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(54) Title: NUCLEIC-ACID BINDING PROTEINS			
(57) Abstract The invention provides human nucleic-acid binding proteins (NuABP) and polynucleotides which identify and encode NuABP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with expression of NuABP.			

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NUCLEIC-ACID BINDING PROTEINS

TECHNICAL FIELD

This invention relates to nucleic acid and amino acid sequences of nucleic-acid binding proteins and to the use of these sequences in the diagnosis, treatment, and prevention of reproductive, immune, and neurological disorders, and cell proliferative disorders including cancer.

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BACKGROUND OF THE INVENTION

Multicellular organisms are comprised of diverse cell types that differ dramatically both in structure and function. The identity of a cell is determined by its characteristic pattern of gene expression, and different cell types express overlapping but distinct sets of genes throughout development. Spatial and temporal regulation of gene expression is critical for the control of cell proliferation, cell differentiation, apoptosis, and other processes that contribute to organismal development. Furthermore, gene expression is regulated in response to extracellular signals that mediate cell-cell communication and coordinate the activities of different cell types. Appropriate gene regulation also ensures that cells function efficiently by expressing only those genes whose functions are required at a given time.

Transcriptional regulatory proteins are essential for the control of gene expression. Some of these proteins function as transcription factors that initiate, activate, repress, or terminate gene transcription. Transcription factors generally bind to promoter, enhancer, or upstream regulatory regions of a gene in a sequence-specific manner, although some factors bind regulatory elements within or downstream of the coding region. Transcription factors may bind to a specific region of DNA singly or as a complex with other accessory factors. (Reviewed in Lewin, B. (1990) Genes IV, Oxford University Press, New York, NY, pp. 554-570.)

The double helix structure and repeated sequences of DNA create topological and chemical features which can be recognized by transcription factors. These features include hydrogen bond donor and acceptor groups, hydrophobic patches, major and minor grooves, and regular repeated stretches of sequence which induce distinct bends in the helix. Typically, transcription factors recognize specific DNA sequence motifs of about 20 nucleotides in length. Multiple adjacent transcription factor-binding motifs may be required for gene regulation.

Many transcription factors incorporate DNA-binding structural motifs which comprise either α helices or β sheets that bind to the major groove of DNA. Four well-characterized structural motifs are helix-turn-helix, zinc finger, leucine zipper, and helix-loop-helix. Proteins containing these motifs may act alone as monomers or form homo- or heterodimers that interact with DNA.

The helix-turn-helix motif consists of two α helices connected at a fixed angle by a short

chain of amino acids. One of the helices binds to the major groove. Helix-turn-helix motifs are exemplified by the homeobox motif which is present in homeodomain proteins. These proteins are critical for specifying the anterior-posterior body axis during development and are conserved throughout the animal kingdom. The Antennapedia and Ultrabithorax proteins of Drosophila melanogaster are prototypical homeodomain proteins. (Pabo, C.O. and R.T. Sauer (1992) Ann. Rev. Biochem. 61:1053-1095.)

The zinc finger motif, which binds zinc ions, generally contains tandem repeats of about 30 amino acids consisting of periodically spaced cysteine and histidine residues. Examples of this sequence pattern include the C2H2-type and the C3HC4-type zinc fingers, and the PHD domain. (Lewin, supra ; Aasland, R., et al. (1995) Trends Biochem. Sci 20:56 - 59.) Zinc finger proteins each contain an α helix and an antiparallel β sheet whose proximity and conformation are maintained by the zinc ion. Contact with DNA is made by the arginine preceding the α helix and by the second, third, and sixth residues of the α helix. Variants of the zinc finger motif include poorly defined cysteine-rich motifs which bind zinc or other metal ions. These motifs may not contain histidine residues and are generally nonrepetitive.

The leucine zipper motif comprises a stretch of amino acids rich in leucine which can form an amphipathic α helix. This structure provides the basis for dimerization of two leucine zipper proteins. The region adjacent to the leucine zipper is usually basic, and upon protein dimerization, is optimally positioned for binding to the major groove. Proteins containing such motifs are generally referred to as bZIP transcription factors.

The helix-loop-helix motif (HLH) consists of a short α helix connected by a loop to a longer α helix. The loop is flexible and allows the two helices to fold back against each other and to bind to DNA. The transcription factor Myc contains a prototypical HLH motif.

Most transcription factors contain characteristic DNA binding motifs, and variations on the above motifs and new motifs have been and are currently being characterized. (Faisst, S. and S. Meyer (1992) Nucl. Acids Res. 20:3-26.)

Mutations in transcription factors contribute to oncogenesis. This is likely due to the role of transcription factors in the expression of genes involved in cell proliferation. For example, mutations in transcription factors encoded by proto-oncogenes, such as Fos, Jun, Myc, Rel, and Sp1, may be oncogenic due to increased stimulation of cell proliferation. Conversely, mutations in transcription factors encoded by tumor suppressor genes, such as p53, RB1, and WT1, may be oncogenic due to decreased inhibition of cell proliferation. (Latchman, D. (1995) Gene Regulation: A Eukaryotic Perspective, Chapman and Hall, London, UK, pp 242-255.)

Gene expression is also affected by chromatin-associated proteins. In the nucleus, DNA is

packaged into chromatin, the compact organization of which limits the accessibility of DNA to transcription factors and plays a key role in gene regulation. (Lewin, supra, pp. 409-410.) The compact structure of chromatin is determined and influenced by chromatin-associated proteins such as histones, high mobility group (HMG) proteins, helicases, and chromodomain proteins. There are five classes of histones, H1, H2A, H2B, H3, and H4, all of which are highly basic, low molecular weight proteins. The fundamental unit of chromatin, the nucleosome, consists of 200 base pairs of DNA associated with two copies each of H2A, H2B, H3, and H4. H1 links adjacent nucleosomes. HMG proteins are low molecular weight, non-histone proteins that may play a role in unwinding DNA and stabilizing single-stranded DNA. Helicases, which are DNA-dependent ATPases, unwind DNA, allowing access for transcription factors. Chromodomain proteins play a key role in the formation of highly-compacted, transcriptionally silent heterochromatin.

Much of the regulation of gene expression in eucaryotic cells occurs at the posttranscriptional level. Messenger RNAs (mRNA), which are produced in the cell nucleus from primary transcripts of protein-encoding genes, are processed and transported to the cytoplasm where the protein synthesis machinery is located. RNA-binding proteins are a group of proteins that participate in the processing, editing, transport, localization, and posttranscriptional regulation of mRNAs, and comprise the protein component of ribosomes as well. The RNA-binding activity of many of these proteins is mediated by a series of RNA-binding motifs identified within them. These domains include the RNP motif, the arginine-rich motif, the RGG box, and the KH motif. (Reviewed in Burd, C. G. and Dreyfuss, G. (1994) *Science* 265:615 - 621.) The RNP motif is the most widely found and best characterized of these motifs. The RNP motif is composed of 90-100 amino acids which form an RNA-binding domain and is found in one or more copies in proteins that bind pre-mRNA, mRNA, pre-ribosomal RNA, and small nuclear RNAs. The RNP motif is composed of two short sequences (RNP-1 and RNP-2) and a number of other mostly hydrophobic, conserved amino acids interspersed throughout the motif. (Burd, supra; ExPASy PROSITE document PDOC0030.)

Many neoplastic disorders in humans can be attributed to inappropriate gene expression. Malignant cell growth may result from either excessive expression of tumor promoting genes or insufficient expression of tumor suppressor genes. (Cleary, M.L. (1992) *Cancer Surv.* 15:89-104.) Chromosomal translocations may also produce chimeric loci which fuse the coding sequence of one gene with the regulatory regions of a second unrelated gene. Such an arrangement often results in inappropriate gene transcription. The Wilms tumor suppressor gene product, WT1, is a protein containing a DNA-binding domain consisting of four zinc fingers and a proline-glutamine rich region capable of regulating transcription. (ExPASy PROSITE document PR00049.) Deletions of the WT1 gene, or point mutations which destroy the DNA-binding activity of the protein are associated with development of the pediatric nephroblastoma, Wilms tumor, and Denys-Drash syndrome. (Rauscher,

F.J. (1993) FASEB J. 7:896-903.)

Certain proteins enriched in glutamine are associated with various neurological disorders including spinocerebellar ataxia, bipolar effective disorder, schizophrenia, and autism. (Margolis, R.L. et al. (1997) Human Genetics 100:114-122.) These proteins contain regions with as many as 15
5 or more consecutive glutamine residues and may function as transcription factors with a potential role in regulation of neurodevelopment or neuroplasticity.

The immune system responds to infection or trauma by activating a cascade of events that coordinate the progressive selection, amplification, and mobilization of cellular defense mechanisms. A complex and balanced program of gene activation and repression is involved in this process.
10 However, hyperactivity of the immune system as a result of improper or insufficient regulation of gene expression may result in considerable tissue or organ damage. This damage is well documented in immunological responses associated with arthritis, allergens, heart attack, stroke, and infections. (Harrison's Principles of Internal Medicine, 13/e, McGraw Hill, Inc. and Teton Data Systems Software, 1996.) In particular, a zinc finger protein termed Staf50 (for Stimulated trans-acting factor
15 of 50 kDa) is a transcriptional regulator and is induced in various cell lines by interferon-I and -II. Staf50 appears to mediate the antiviral activity of interferon by down-regulating the viral transcription directed by the long terminal repeat promoter region of human immunodeficiency virus type-1 in transfected cells. (Tissot, C. (1995) J. Biol. Chem. 270:14891-14898.)

Furthermore, the generation of multicellular organisms is based upon the induction and
20 coordination of cell differentiation at the appropriate stages of development. Central to this process is differential gene expression, which confers the distinct identities of cells and tissues throughout the body. Failure to regulate gene expression during development could result in developmental disorders.

The discovery of new nucleic-acid binding proteins and the polynucleotides encoding them
25 satisfies a need in the art by providing new compositions which are useful in the diagnosis, prevention, and treatment of reproductive, immune, and neurological disorders, and cell proliferative disorders including cancer.

SUMMARY OF THE INVENTION

30 The invention features purified polypeptides, protnames, referred to collectively as "ABBR" and individually as "NuABP-1," "NuABP-2," "NuABP-3," "NuABP-4," "NuABP-5," "NuABP-6," "NuABP-7," "NuABP-8," "NuABP-9," "NuABP-10," "NuABP-11," "NuABP-12," "NuABP-13," "NuABP-14," "NuABP-15," "NuABP-16," "NuABP-17," "NuABP-18," "NuABP-19," "NuABP-20," "NuABP-21," "NuABP-22," "NuABP-23," "NuABP-24," "NuABP-25," "NuABP-26," "NuABP-
35 27," "NuABP-28," "NuABP-29," "NuABP-30," "NuABP-31," "NuABP-32," "NuABP-33,"

"NuABP-34," "NuABP-35," "NuABP-36," "NuABP-37," "NuABP-38," "NuABP-39," "NuABP-40," "NuABP-41," "NuABP-42," "NuABP-43," "NuABP-44," "NuABP-45," "NuABP-46," "NuABP-47," "NuABP-48," "NuABP-49," "NuABP-50," "NuABP-51," "NuABP-52," "NuABP-53," "NuABP-54," and "NuABP-55." In one aspect, the invention provides an isolated polypeptide comprising a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, or d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-55. In one alternative, the invention provides an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:1-55.

The invention further provides an isolated polynucleotide encoding a polypeptide comprising a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, or d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-55. In one alternative, the polynucleotide is selected from the group consisting of SEQ ID NO:56-110.

Additionally, the invention provides a recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide encoding a polypeptide comprising a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, or d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-55. In one alternative, the invention provides a cell transformed with the recombinant polynucleotide. In another alternative, the invention provides a transgenic organism comprising the recombinant polynucleotide.

The invention also provides a method for producing a polypeptide comprising a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, or d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-55. The method comprises a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide encoding the polypeptide, and b) recovering the polypeptide so expressed.

Additionally, the invention provides an isolated antibody which specifically binds to a polypeptide comprising a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, c) a biologically active
5 fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, or d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-55.

The invention further provides an isolated polynucleotide comprising a) a polynucleotide sequence selected from the group consisting of SEQ ID NO:56-110, b) a naturally occurring
10 polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:56-110, c) a polynucleotide sequence complementary to a), or d) a polynucleotide sequence complementary to b). In one alternative, the polynucleotide comprises at least 60 contiguous nucleotides.

Additionally, the invention provides a method for detecting a target polynucleotide in a
15 sample, said target polynucleotide having a sequence of a polynucleotide comprising a) a polynucleotide sequence selected from the group consisting of SEQ ID NO:56-110, b) a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:56-110, c) a polynucleotide sequence complementary to a), or d) a polynucleotide sequence complementary to b). The method comprises a)
20 hybridizing the sample with a probe comprising at least 16 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide, and b) detecting the presence or absence of said hybridization complex, and optionally, if present, the amount thereof. In one alternative, the probe
25 comprises at least 30 contiguous nucleotides. In another alternative, the probe comprises at least 60 contiguous nucleotides.

The invention further provides a pharmaceutical composition comprising an effective amount of a polypeptide comprising a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an
30 amino acid sequence selected from the group consisting of SEQ ID NO:1-55, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, or d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, and a pharmaceutically acceptable excipient. The invention additionally provides a method of treating a disease or condition associated with decreased expression of functional NuABP,
35 comprising administering to a patient in need of such treatment the pharmaceutical composition.

The invention also provides a method for screening a compound for effectiveness as an agonist of a polypeptide comprising a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, or d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-55. The method comprises a) exposing a sample comprising the polypeptide to a compound, and b) detecting agonist activity in the sample. In one alternative, the invention provides a pharmaceutical composition comprising an agonist compound identified by the method and a pharmaceutically acceptable excipient. In another alternative, the invention provides a method of treating a disease or condition associated with decreased expression of functional NuABP, comprising administering to a patient in need of such treatment the pharmaceutical composition.

Additionally, the invention provides a method for screening a compound for effectiveness as an antagonist of a polypeptide comprising a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-55, or d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-55. The method comprises a) exposing a sample comprising the polypeptide to a compound, and b) detecting antagonist activity in the sample. In one alternative, the invention provides a pharmaceutical composition comprising an antagonist compound identified by the method and a pharmaceutically acceptable excipient. In another alternative, the invention provides a method of treating a disease or condition associated with overexpression of functional NuABP, comprising administering to a patient in need of such treatment the pharmaceutical composition.

The invention further provides a method for screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence selected from the group consisting of SEQ ID NO:56-110, the method comprising a) exposing a sample comprising the target polynucleotide to a compound, and b) detecting altered expression of the target polynucleotide.

BRIEF DESCRIPTION OF THE TABLES

Table 1 shows polypeptide and nucleotide sequence identification numbers (SEQ ID NOs), clone identification numbers (clone IDs), cDNA libraries, and cDNA fragments used to assemble full-length sequences encoding NuABP.

Table 2 shows features of each polypeptide sequence, including potential motifs, homologous sequences, and methods, algorithms, and searchable databases used for analysis of NuABP.

Table 3 shows selected fragments of each nucleic acid sequence; the tissue-specific expression patterns of each nucleic acid sequence as determined by northern analysis; diseases, disorders, or conditions associated with these tissues; and the vector into which each cDNA was cloned.

Table 4 describes the tissues used to construct the cDNA libraries from which cDNA clones encoding NuABP were isolated.

Table 5 shows the tools, programs, and algorithms used to analyze NuABP, along with applicable descriptions, references, and threshold parameters.

DESCRIPTION OF THE INVENTION

Before the present proteins, nucleotide sequences, and methods are described, it is understood that this invention is not limited to the particular machines, materials and methods described, as these may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to limit the scope of the present invention which will be limited only by the appended claims.

It must be noted that as used herein and in the appended claims, the singular forms "a," "an," and "the" include plural reference unless the context clearly dictates otherwise. Thus, for example, a reference to "a host cell" includes a plurality of such host cells, and a reference to "an antibody" is a reference to one or more antibodies and equivalents thereof known to those skilled in the art, and so forth.

Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art to which this invention belongs. Although any machines, materials, and methods similar or equivalent to those described herein can be used to practice or test the present invention, the preferred machines, materials and methods are now described. All publications mentioned herein are cited for the purpose of describing and disclosing the cell lines, protocols, reagents and vectors which are reported in the publications and which might be used in connection with the invention. Nothing herein is to be construed as an admission that the invention is not entitled to antedate such disclosure by virtue of prior invention.

DEFINITIONS

"NuABP" refers to the amino acid sequences of substantially purified NuABP obtained from any species, particularly a mammalian species, including bovine, ovine, porcine, murine, equine, and human, and from any source, whether natural, synthetic, semi-synthetic, or recombinant.

The term "agonist" refers to a molecule which intensifies or mimics the biological activity of

NuABP. Agonists may include proteins, nucleic acids, carbohydrates, small molecules, or any other compound or composition which modulates the activity of NuABP either by directly interacting with NuABP or by acting on components of the biological pathway in which NuABP participates.

An "allelic variant" is an alternative form of the gene encoding NuABP. Allelic variants may result from at least one mutation in the nucleic acid sequence and may result in altered mRNAs or in polypeptides whose structure or function may or may not be altered. A gene may have none, one, or many allelic variants of its naturally occurring form. Common mutational changes which give rise to allelic variants are generally ascribed to natural deletions, additions, or substitutions of nucleotides. Each of these types of changes may occur alone, or in combination with the others, one or more times in a given sequence.

"Altered" nucleic acid sequences encoding NuABP include those sequences with deletions, insertions, or substitutions of different nucleotides, resulting in a polypeptide the same as NuABP or a polypeptide with at least one functional characteristic of NuABP. Included within this definition are polymorphisms which may or may not be readily detectable using a particular oligonucleotide probe of the polynucleotide encoding NuABP, and improper or unexpected hybridization to allelic variants, with a locus other than the normal chromosomal locus for the polynucleotide sequence encoding NuABP. The encoded protein may also be "altered," and may contain deletions, insertions, or substitutions of amino acid residues which produce a silent change and result in a functionally equivalent NuABP. Deliberate amino acid substitutions may be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues, as long as the biological or immunological activity of NuABP is retained. For example, negatively charged amino acids may include aspartic acid and glutamic acid, and positively charged amino acids may include lysine and arginine. Amino acids with uncharged polar side chains having similar hydrophilicity values may include: asparagine and glutamine; and serine and threonine. Amino acids with uncharged side chains having similar hydrophilicity values may include: leucine, isoleucine, and valine; glycine and alanine; and phenylalanine and tyrosine.

The terms "amino acid" and "amino acid sequence" refer to an oligopeptide, peptide, polypeptide, or protein sequence, or a fragment of any of these, and to naturally occurring or synthetic molecules. Where "amino acid sequence" is recited to refer to an amino acid sequence of a naturally occurring protein molecule, "amino acid sequence" and like terms are not meant to limit the amino acid sequence to the complete native amino acid sequence associated with the recited protein molecule.

"Amplification" relates to the production of additional copies of a nucleic acid sequence. Amplification is generally carried out using polymerase chain reaction (PCR) technologies well known in the art.

The term "antagonist" refers to a molecule which inhibits or attenuates the biological activity of NuABP. Antagonists may include proteins such as antibodies, nucleic acids, carbohydrates, small molecules, or any other compound or composition which modulates the activity of NuABP either by directly interacting with NuABP or by acting on components of the biological pathway in which NuABP participates.

The term "antibody" refers to intact immunoglobulin molecules as well as to fragments thereof, such as Fab, F(ab')₂, and Fv fragments, which are capable of binding an epitopic determinant. Antibodies that bind NuABP polypeptides can be prepared using intact polypeptides or using fragments containing small peptides of interest as the immunizing antigen. The polypeptide or oligopeptide used to immunize an animal (e.g., a mouse, a rat, or a rabbit) can be derived from the translation of RNA, or synthesized chemically, and can be conjugated to a carrier protein if desired. Commonly used carriers that are chemically coupled to peptides include bovine serum albumin, thyroglobulin, and keyhole limpet hemocyanin (KLH). The coupled peptide is then used to immunize the animal.

The term "antigenic determinant" refers to that region of a molecule (i.e., an epitope) that makes contact with a particular antibody. When a protein or a fragment of a protein is used to immunize a host animal, numerous regions of the protein may induce the production of antibodies which bind specifically to antigenic determinants (particular regions or three-dimensional structures on the protein). An antigenic determinant may compete with the intact antigen (i.e., the immunogen used to elicit the immune response) for binding to an antibody.

The term "antisense" refers to any composition containing a nucleic acid sequence which is complementary to the "sense" strand of a specific nucleic acid sequence. Antisense molecules may be produced by any method including synthesis or transcription. Once introduced into a cell, the complementary nucleotides combine with natural sequences produced by the cell to form duplexes and to block either transcription or translation. The designation "negative" or "minus" can refer to the antisense strand, and the designation "positive" or "plus" can refer to the sense strand.

The term "biologically active" refers to a protein having structural, regulatory, or biochemical functions of a naturally occurring molecule. Likewise, "immunologically active" refers to the capability of the natural, recombinant, or synthetic NuABP, or of any oligopeptide thereof, to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies.

The terms "complementary" and "complementarity" refer to the natural binding of polynucleotides by base pairing. For example, the sequence "5' A-G-T 3'" bonds to the complementary sequence "3' T-C-A 5'." Complementarity between two single-stranded molecules may be "partial," such that only some of the nucleic acids bind, or it may be "complete," such that total complementarity exists between the single stranded molecules. The degree of complementarity

between nucleic acid strands has significant effects on the efficiency and strength of the hybridization between the nucleic acid strands. This is of particular importance in amplification reactions, which depend upon binding between nucleic acid strands, and in the design and use of peptide nucleic acid (PNA) molecules.

5 A "composition comprising a given polynucleotide sequence" and a "composition comprising a given amino acid sequence" refer broadly to any composition containing the given polynucleotide or amino acid sequence. The composition may comprise a dry formulation or an aqueous solution. Compositions comprising polynucleotide sequences encoding NuABP or fragments of NuABP may be employed as hybridization probes. The probes may be stored in freeze-dried form and may be
10 associated with a stabilizing agent such as a carbohydrate. In hybridizations, the probe may be deployed in an aqueous solution containing salts (e.g., NaCl), detergents (e.g., sodium dodecyl sulfate; SDS), and other components (e.g., Denhardt's solution, dry milk, salmon sperm DNA, etc.).

"Consensus sequence" refers to a nucleic acid sequence which has been resequenced to resolve uncalled bases, extended using the XL-PCR kit (Perkin-Elmer, Norwalk CT) in the 5' and/or
15 the 3' direction, and resequenced, or which has been assembled from the overlapping sequences of one or more Incyte Clones and, in some cases, one or more public domain ESTs, using a computer program for fragment assembly, such as the GELVIEW fragment assembly system (GCG, Madison WI). Some sequences have been both extended and assembled to produce the consensus sequence.

"Conservative amino acid substitutions" are those substitutions that, when made, least
20 interfere with the properties of the original protein, i.e., the structure and especially the function of the protein is conserved and not significantly changed by such substitutions. The table below shows amino acids which may be substituted for an original amino acid in a protein and which are regarded as conservative amino acid substitutions.

	Original Residue	Conservative Substitution
25	Ala	Gly, Ser
	Arg	His, Lys
	Asn	Asp, Gln, His
	Asp	Asn, Glu
	Cys	Ala, Ser
30	Gln	Asn, Glu, His
	Glu	Asp, Gln, His
	Gly	Ala
	His	Asn, Arg, Gln, Glu
	Ile	Leu, Val
35	Leu	Ile, Val
	Lys	Arg, Gln, Glu
	Met	Leu, Ile
	Phe	His, Met, Leu, Trp, Tyr
	Ser	Cys, Thr
40	Thr	Ser, Val

Trp
Tyr
Val

Phe, Tyr
His, Phe, Trp
Ile, Leu, Thr

5 Conservative amino acid substitutions generally maintain (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a beta sheet or alpha helical conformation, (b) the charge or hydrophobicity of the molecule at the site of the substitution, and/or (c) the bulk of the side chain.

10 A "deletion" refers to a change in the amino acid or nucleotide sequence that results in the absence of one or more amino acid residues or nucleotides.

15 The term "derivative" refers to the chemical modification of a polypeptide sequence, or a polynucleotide sequence. Chemical modifications of a polynucleotide sequence can include, for example, replacement of hydrogen by an alkyl, acyl, hydroxyl, or amino group. A derivative polynucleotide encodes a polypeptide which retains at least one biological or immunological function of the natural molecule. A derivative polypeptide is one modified by glycosylation, pegylation, or any similar process that retains at least one biological or immunological function of the polypeptide from which it was derived.

20 A "fragment" is a unique portion of NuABP or the polynucleotide encoding NuABP which is identical in sequence to but shorter in length than the parent sequence. A fragment may comprise up to the entire length of the defined sequence, minus one nucleotide/amino acid residue. For example, a fragment may comprise from 5 to 1000 contiguous nucleotides or amino acid residues. A fragment used as a probe, primer, antigen, therapeutic molecule, or for other purposes, may be at least 5, 10, 15, 20, 25, 30, 40, 50, 60, 75, 100, 150, 250 or at least 500 contiguous nucleotides or amino acid residues in length. Fragments may be preferentially selected from certain regions of a molecule. For example,

25 a polypeptide fragment may comprise a certain length of contiguous amino acids selected from the first 250 or 500 amino acids (or first 25% or 50% of a polypeptide) as shown in a certain defined sequence. Clearly these lengths are exemplary, and any length that is supported by the specification, including the Sequence Listing, tables, and figures, may be encompassed by the present embodiments.

30 A fragment of SEQ ID NO:56-110 comprises a region of unique polynucleotide sequence that specifically identifies SEQ ID NO:56-110, for example, as distinct from any other sequence in the same genome. A fragment of SEQ ID NO:56-110 is useful, for example, in hybridization and amplification technologies and in analogous methods that distinguish SEQ ID NO:56-110 from related polynucleotide sequences. The precise length of a fragment of SEQ ID NO:56-110 and the region of SEQ ID NO:56-110 to which the fragment corresponds are routinely determinable by one of

35 ordinary skill in the art based on the intended purpose for the fragment.

 A fragment of SEQ ID NO:1-55 is encoded by a fragment of SEQ ID NO:56-110. A

fragment of SEQ ID NO:1-55 comprises a region of unique amino acid sequence that specifically identifies SEQ ID NO:1-55. For example, a fragment of SEQ ID NO:1-55 is useful as an immunogenic peptide for the development of antibodies that specifically recognize SEQ ID NO:1-55. The precise length of a fragment of SEQ ID NO:1-55 and the region of SEQ ID NO:1-55 to which the
5 fragment corresponds are routinely determinable by one of ordinary skill in the art based on the intended purpose for the fragment.

The term "similarity" refers to a degree of complementarity. There may be partial similarity or complete similarity. The word "identity" may substitute for the word "similarity." A partially complementary sequence that at least partially inhibits an identical sequence from hybridizing to a
10 target nucleic acid is referred to as "substantially similar." The inhibition of hybridization of the completely complementary sequence to the target sequence may be examined using a hybridization assay (Southern or northern blot, solution hybridization, and the like) under conditions of reduced stringency. A substantially similar sequence or hybridization probe will compete for and inhibit the binding of a completely similar (identical) sequence to the target sequence under conditions of
15 reduced stringency. This is not to say that conditions of reduced stringency are such that non-specific binding is permitted, as reduced stringency conditions require that the binding of two sequences to one another be a specific (i.e., a selective) interaction. The absence of non-specific binding may be tested by the use of a second target sequence which lacks even a partial degree of complementarity (e.g., less than about 30% similarity or identity). In the absence of non-specific binding, the
20 substantially similar sequence or probe will not hybridize to the second non-complementary target sequence.

The phrases "percent identity" and "% identity," as applied to polynucleotide sequences, refer to the percentage of residue matches between at least two polynucleotide sequences aligned using a standardized algorithm. Such an algorithm may insert, in a standardized and reproducible way, gaps
25 in the sequences being compared in order to optimize alignment between two sequences, and therefore achieve a more meaningful comparison of the two sequences.

Percent identity between polynucleotide sequences may be determined using the default parameters of the CLUSTAL V algorithm as incorporated into the MEGALIGN version 3.12e sequence alignment program. This program is part of the LASERGENE software package, a suite of
30 molecular biological analysis programs (DNASTAR, Madison WI). CLUSTAL V is described in Higgins, D.G. and P.M. Sharp (1989) CABIOS 5:151-153 and in Higgins, D.G. et al. (1992) CABIOS 8:189-191. For pairwise alignments of polynucleotide sequences, the default parameters are set as follows: Ktuple=2, gap penalty=5, window=4, and "diagonals saved"=4. The "weighted" residue weight table is selected as the default. Percent identity is reported by CLUSTAL V as the "percent
35 similarity" between aligned polynucleotide sequence pairs.

Alternatively, a suite of commonly used and freely available sequence comparison algorithms is provided by the National Center for Biotechnology Information (NCBI) Basic Local Alignment Search Tool (BLAST) (Altschul, S.F. et al. (1990) J. Mol. Biol. 215:403-410), which is available from several sources, including the NCBI, Bethesda, MD, and on the Internet at

5 <http://www.ncbi.nlm.nih.gov/BLAST/>. The BLAST software suite includes various sequence analysis programs including "blastn," that is used to align a known polynucleotide sequence with other polynucleotide sequences from a variety of databases. Also available is a tool called "BLAST 2 Sequences" that is used for direct pairwise comparison of two nucleotide sequences. "BLAST 2 Sequences" can be accessed and used interactively at <http://www.ncbi.nlm.nih.gov/gorf/bl2.html>. The

10 "BLAST 2 Sequences" tool can be used for both blastn and blastp (discussed below). BLAST programs are commonly used with gap and other parameters set to default settings. For example, to compare two nucleotide sequences, one may use blastn with the "BLAST 2 Sequences" tool Version 2.0.9 (May-07-1999) set at default parameters. Such default parameters may be, for example:

Matrix: BLOSUM62

15 *Reward for match: 1*

Penalty for mismatch: -2

Open Gap: 5 and Extension Gap: 2 penalties

Gap x drop-off: 50

Expect: 10

20 *Word Size: 11*

Filter: on

Percent identity may be measured over the length of an entire defined sequence, for example, as defined by a particular SEQ ID number, or may be measured over a shorter length, for example, over the length of a fragment taken from a larger, defined sequence, for instance, a fragment of at

25 least 20, at least 30, at least 40, at least 50, at least 70, at least 100, or at least 200 contiguous nucleotides. Such lengths are exemplary only, and it is understood that any fragment length supported by the sequences shown herein, in the tables, figures, or Sequence Listing, may be used to describe a length over which percentage identity may be measured.

Nucleic acid sequences that do not show a high degree of identity may nevertheless encode

30 similar amino acid sequences due to the degeneracy of the genetic code. It is understood that changes in a nucleic acid sequence can be made using this degeneracy to produce multiple nucleic acid sequences that all encode substantially the same protein.

The phrases "percent identity" and "% identity," as applied to polypeptide sequences, refer to the percentage of residue matches between at least two polypeptide sequences aligned using a

35 standardized algorithm. Methods of polypeptide sequence alignment are well-known. Some

alignment methods take into account conservative amino acid substitutions. Such conservative substitutions, explained in more detail above, generally preserve the hydrophobicity and acidity at the site of substitution, thus preserving the structure (and therefore function) of the polypeptide.

Percent identity between polypeptide sequences may be determined using the default parameters of the CLUSTAL V algorithm as incorporated into the MEGALIGN version 3.12e sequence alignment program (described and referenced above). For pairwise alignments of polypeptide sequences using CLUSTAL V, the default parameters are set as follows: Ktuple=1, gap penalty=3, window=5, and "diagonals saved"=5. The PAM250 matrix is selected as the default residue weight table. As with polynucleotide alignments, the percent identity is reported by CLUSTAL V as the "percent similarity" between aligned polypeptide sequence pairs.

Alternatively the NCBI BLAST software suite may be used. For example, for a pairwise comparison of two polypeptide sequences, one may use the "BLAST 2 Sequences" tool Version 2.0.9 (May-07-1999) with blastp set at default parameters. Such default parameters may be, for example:

Matrix: BLOSUM62

Open Gap: 11 and Extension Gap: 1 penalties

Gap x drop-off: 50

Expect: 10

Word Size: 3

Filter: on

Percent identity may be measured over the length of an entire defined polypeptide sequence, for example, as defined by a particular SEQ ID number, or may be measured over a shorter length, for example, over the length of a fragment taken from a larger, defined polypeptide sequence, for instance, a fragment of at least 15, at least 20, at least 30, at least 40, at least 50, at least 70 or at least 150 contiguous residues. Such lengths are exemplary only, and it is understood that any fragment length supported by the sequences shown herein, in the tables, figures or Sequence Listing, may be used to describe a length over which percentage identity may be measured.

"Human artificial chromosomes" (HACs) are linear microchromosomes which may contain DNA sequences of about 6 kb to 10 Mb in size, and which contain all of the elements required for stable mitotic chromosome segregation and maintenance.

The term "humanized antibody" refers to antibody molecules in which the amino acid sequence in the non-antigen binding regions has been altered so that the antibody more closely resembles a human antibody, and still retains its original binding ability.

"Hybridization" refers to the process by which a polynucleotide strand anneals with a complementary strand through base pairing under defined hybridization conditions. Specific hybridization is an indication that two nucleic acid sequences share a high degree of identity. Specific

hybridization complexes form under permissive annealing conditions and remain hybridized after the "washing" step(s). The washing step(s) is particularly important in determining the stringency of the hybridization process, with more stringent conditions allowing less non-specific binding, i.e., binding between pairs of nucleic acid strands that are not perfectly matched. Permissive conditions for
5 annealing of nucleic acid sequences are routinely determinable by one of ordinary skill in the art and may be consistent among hybridization experiments, whereas wash conditions may be varied among experiments to achieve the desired stringency, and therefore hybridization specificity. Permissive annealing conditions occur, for example, at 68°C in the presence of about 6 x SSC, about 1% (w/v) SDS, and about 100 µg/ml denatured salmon sperm DNA.

10 Generally, stringency of hybridization is expressed, in part, with reference to the temperature under which the wash step is carried out. Generally, such wash temperatures are selected to be about 5°C to 20°C lower than the thermal melting point (T_m) for the specific sequence at a defined ionic strength and pH. The T_m is the temperature (under defined ionic strength and pH) at which 50% of the target sequence hybridizes to a perfectly matched probe. An equation for calculating T_m and
15 conditions for nucleic acid hybridization are well known and can be found in Sambrook et al., 1989, Molecular Cloning: A Laboratory Manual, 2nd ed., vol. 1-3, Cold Spring Harbor Press, Plainview NY; specifically see volume 2, chapter 9.

High stringency conditions for hybridization between polynucleotides of the present invention include wash conditions of 68°C in the presence of about 0.2 x SSC and about 0.1% SDS, for 1 hour.
20 Alternatively, temperatures of about 65°C, 60°C, 55°C, or 42°C may be used. *SSC concentration may be varied from about 0.1 to 2 x SSC, with SDS being present at about 0.1%. Typically, blocking reagents are used to block non-specific hybridization. Such blocking reagents include, for instance, denatured salmon sperm DNA at about 100-200 µg/ml. Organic solvent, such as formamide at a concentration of about 35-50% v/v, may also be used under particular circumstances, such as for
25 RNA:DNA hybridizations. Useful variations on these wash conditions will be readily apparent to those of ordinary skill in the art. Hybridization, particularly under high stringency conditions, may be suggestive of evolutionary similarity between the nucleotides. Such similarity is strongly indicative of a similar role for the nucleotides and their encoded polypeptides.

The term "hybridization complex" refers to a complex formed between two nucleic acid
30 sequences by virtue of the formation of hydrogen bonds between complementary bases. A hybridization complex may be formed in solution (e.g., C_0t or R_0t analysis) or formed between one nucleic acid sequence present in solution and another nucleic acid sequence immobilized on a solid support (e.g., paper, membranes, filters, chips, pins or glass slides, or any other appropriate substrate to which cells or their nucleic acids have been fixed).

35 The words "insertion" and "addition" refer to changes in an amino acid or nucleotide

sequence resulting in the addition of one or more amino acid residues or nucleotides, respectively.

"Immune response" can refer to conditions associated with inflammation, trauma, immune disorders, or infectious or genetic disease, etc. These conditions can be characterized by expression of various factors, e.g., cytokines, chemokines, and other signaling molecules, which may affect
5 cellular and systemic defense systems.

The term "microarray" refers to an arrangement of distinct polynucleotides on a substrate.

The terms "element" and "array element" in a microarray context, refer to hybridizable polynucleotides arranged on the surface of a substrate.

The term "modulate" refers to a change in the activity of NuABP. For example, modulation
10 may cause an increase or a decrease in protein activity, binding characteristics, or any other biological, functional, or immunological properties of NuABP.

The phrases "nucleic acid" and "nucleic acid sequence" refer to a nucleotide, oligonucleotide, polynucleotide, or any fragment thereof. These phrases also refer to DNA or RNA of genomic or synthetic origin which may be single-stranded or double-stranded and may represent the sense or the
15 antisense strand, to peptide nucleic acid (PNA), or to any DNA-like or RNA-like material.

"Operably linked" refers to the situation in which a first nucleic acid sequence is placed in a functional relationship with the second nucleic acid sequence. For instance, a promoter is operably linked to a coding sequence if the promoter affects the transcription or expression of the coding sequence. Generally, operably linked DNA sequences may be in close proximity or contiguous and,
20 where necessary to join two protein coding regions, in the same reading frame.

"Peptide nucleic acid" (PNA) refers to an antisense molecule or anti-gene agent which comprises an oligonucleotide of at least about 5 nucleotides in length linked to a peptide backbone of amino acid residues ending in lysine. The terminal lysine confers solubility to the composition. PNAs preferentially bind complementary single stranded DNA or RNA and stop transcript elongation,
25 and may be pegylated to extend their lifespan in the cell.

"Probe" refers to nucleic acid sequences encoding NuABP, their complements, or fragments thereof, which are used to detect identical, allelic or related nucleic acid sequences. Probes are isolated oligonucleotides or polynucleotides attached to a detectable label or reporter molecule. Typical labels include radioactive isotopes, ligands, chemiluminescent agents, and enzymes.

30 "Primers" are short nucleic acids, usually DNA oligonucleotides, which may be annealed to a target polynucleotide by complementary base-pairing. The primer may then be extended along the target DNA strand by a DNA polymerase enzyme. Primer pairs can be used for amplification (and identification) of a nucleic acid sequence, e.g., by the polymerase chain reaction (PCR).

Probes and primers as used in the present invention typically comprise at least 15 contiguous
35 nucleotides of a known sequence. In order to enhance specificity, longer probes and primers may also

be employed, such as probes and primers that comprise at least 20, 25, 30, 40, 50, 60, 70, 80, 90, 100, or at least 150 consecutive nucleotides of the disclosed nucleic acid sequences. Probes and primers may be considerably longer than these examples, and it is understood that any length supported by the specification, including the tables, figures, and Sequence Listing, may be used.

5 Methods for preparing and using probes and primers are described in the references, for example Sambrook et al., 1989, Molecular Cloning: A Laboratory Manual, 2nd ed., vol. 1-3, Cold Spring Harbor Press, Plainview NY; Ausubel et al., 1987, Current Protocols in Molecular Biology, Greene Publ. Assoc. & Wiley-Intersciences, New York NY; Innis et al., 1990, PCR Protocols. A Guide to Methods and Applications, Academic Press, San Diego CA. PCR primer pairs can be
10 derived from a known sequence, for example, by using computer programs intended for that purpose such as Primer (Version 0.5, 1991, Whitehead Institute for Biomedical Research, Cambridge MA).

 Oligonucleotides for use as primers are selected using software known in the art for such purpose. For example, OLIGO 4.06 software is useful for the selection of PCR primer pairs of up to 100 nucleotides each, and for the analysis of oligonucleotides and larger polynucleotides of up to
15 5,000 nucleotides from an input polynucleotide sequence of up to 32 kilobases. Similar primer selection programs have incorporated additional features for expanded capabilities. For example, the PrimOU primer selection program (available to the public from the Genome Center at University of Texas South West Medical Center, Dallas TX) is capable of choosing specific primers from megabase sequences and is thus useful for designing primers on a genome-wide scope. The Primer3 primer
20 selection program (available to the public from the Whitehead Institute/MIT Center for Genome Research, Cambridge MA) allows the user to input a "mispriming library," in which sequences to avoid as primer binding sites are user-specified. Primer3 is useful, in particular, for the selection of oligonucleotides for microarrays. (The source code for the latter two primer selection programs may also be obtained from their respective sources and modified to meet the user's specific needs.) The
25 PrimeGen program (available to the public from the UK Human Genome Mapping Project Resource Centre, Cambridge UK) designs primers based on multiple sequence alignments, thereby allowing selection of primers that hybridize to either the most conserved or least conserved regions of aligned nucleic acid sequences. Hence, this program is useful for identification of both unique and conserved oligonucleotides and polynucleotide fragments. The oligonucleotides and polynucleotide fragments
30 identified by any of the above selection methods are useful in hybridization technologies, for example, as PCR or sequencing primers, microarray elements, or specific probes to identify fully or partially complementary polynucleotides in a sample of nucleic acids. Methods of oligonucleotide selection are not limited to those described above.

 A "recombinant nucleic acid" is a sequence that is not naturally occurring or has a sequence
35 that is made by an artificial combination of two or more otherwise separated segments of sequence.

This artificial combination is often accomplished by chemical synthesis or, more commonly, by the artificial manipulation of isolated segments of nucleic acids, e.g., by genetic engineering techniques such as those described in Sambrook, *supra*. The term recombinant includes nucleic acids that have been altered solely by addition, substitution, or deletion of a portion of the nucleic acid. Frequently, a recombinant nucleic acid may include a nucleic acid sequence operably linked to a promoter sequence. Such a recombinant nucleic acid may be part of a vector that is used, for example, to transform a cell.

Alternatively, such recombinant nucleic acids may be part of a viral vector, e.g., based on a vaccinia virus, that could be used to vaccinate a mammal wherein the recombinant nucleic acid is expressed, inducing a protective immunological response in the mammal.

The term "sample" is used in its broadest sense. A sample suspected of containing nucleic acids encoding NuABP, or fragments thereof, or NuABP itself, may comprise a bodily fluid; an extract from a cell, chromosome, organelle, or membrane isolated from a cell; a cell; genomic DNA, RNA, or cDNA, in solution or bound to a substrate; a tissue; a tissue print; etc.

The terms "specific binding" and "specifically binding" refer to that interaction between a protein or peptide and an agonist, an antibody, an antagonist, a small molecule, or any natural or synthetic binding composition. The interaction is dependent upon the presence of a particular structure of the protein, e.g., the antigenic determinant or epitope, recognized by the binding molecule. For example, if an antibody is specific for epitope "A," the presence of a polypeptide containing the epitope A, or the presence of free unlabeled A, in a reaction containing free labeled A and the antibody will reduce the amount of labeled A that binds to the antibody.

The term "substantially purified" refers to nucleic acid or amino acid sequences that are removed from their natural environment and are isolated or separated, and are at least 60% free, preferably at least 75% free, and most preferably at least 90% free from other components with which they are naturally associated.

A "substitution" refers to the replacement of one or more amino acids or nucleotides by different amino acids or nucleotides, respectively.

"Substrate" refers to any suitable rigid or semi-rigid support including membranes, filters, chips, slides, wafers, fibers, magnetic or nonmagnetic beads, gels, tubing, plates, polymers, microparticles and capillaries. The substrate can have a variety of surface forms, such as wells, trenches, pins, channels and pores, to which polynucleotides or polypeptides are bound.

"Transformation" describes a process by which exogenous DNA enters and changes a recipient cell. Transformation may occur under natural or artificial conditions according to various methods well known in the art, and may rely on any known method for the insertion of foreign nucleic acid sequences into a prokaryotic or eukaryotic host cell. The method for transformation is selected

based on the type of host cell being transformed and may include, but is not limited to, viral infection, electroporation, heat shock, lipofection, and particle bombardment. The term "transformed" cells includes stably transformed cells in which the inserted DNA is capable of replication either as an autonomously replicating plasmid or as part of the host chromosome, as well as transiently transformed cells which express the inserted DNA or RNA for limited periods of time.

A "variant" of a particular nucleic acid sequence is defined as a nucleic acid sequence having at least 40% sequence identity to the particular nucleic acid sequence over a certain length of one of the nucleic acid sequences using blastn with the "BLAST 2 Sequences" tool Version 2.0.9 (May-07-1999) set at default parameters. Such a pair of nucleic acids may show, for example, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95% or at least 98% or greater sequence identity over a certain defined length. A variant may be described as, for example, an "allelic" (as defined above), "splice," "species," or "polymorphic" variant. A splice variant may have significant identity to a reference molecule, but will generally have a greater or lesser number of polynucleotides due to alternate splicing of exons during mRNA processing. The corresponding polypeptide may possess additional functional domains or lack domains that are present in the reference molecule. Species variants are polynucleotide sequences that vary from one species to another. The resulting polypeptides generally will have significant amino acid identity relative to each other. A polymorphic variant is a variation in the polynucleotide sequence of a particular gene between individuals of a given species. Polymorphic variants also may encompass "single nucleotide polymorphisms" (SNPs) in which the polynucleotide sequence varies by one nucleotide base. The presence of SNPs may be indicative of, for example, a certain population, a disease state, or a propensity for a disease state.

A "variant" of a particular polypeptide sequence is defined as a polypeptide sequence having at least 40% sequence identity to the particular polypeptide sequence over a certain length of one of the polypeptide sequences using blastp with the "BLAST 2 Sequences" tool Version 2.0.9 (May-07-1999) set at default parameters. Such a pair of polypeptides may show, for example, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, or at least 98% or greater sequence identity over a certain defined length of one of the polypeptides.

30 THE INVENTION

The invention is based on the discovery of new human nucleic-acid binding proteins (NuABP), the polynucleotides encoding NuABP, and the use of these compositions for the diagnosis, treatment, or prevention of reproductive, immune, and neurological disorders, and cell proliferative disorders including cancer.

35 Table 1 lists the Incyte clones used to assemble full length nucleotide sequences encoding

NuABP. Columns 1 and 2 show the sequence identification numbers (SEQ ID NOs) of the polypeptide and nucleotide sequences, respectively. Column 3 shows the clone IDs of the Incyte clones in which nucleic acids encoding each NuABP were identified, and column 4 shows the cDNA libraries from which these clones were isolated. Column 5 shows Incyte clones and their
 5 corresponding cDNA libraries. Clones for which cDNA libraries are not indicated were derived from pooled cDNA libraries. The Incyte clones in column 5 were used to assemble the consensus nucleotide sequence of each NuABP and are useful as fragments in hybridization technologies.

The columns of Table 2 show various properties of each of the polypeptides of the invention: column 1 references the SEQ ID NO; column 2 shows the number of amino acid residues in each
 10 polypeptide; column 3 shows potential phosphorylation sites; column 4 shows potential glycosylation sites; column 5 shows the amino acid residues comprising signature sequences and motifs; column 6 shows identification or homologous sequences as identified by BLAST analysis; and column 7 shows analytical methods and in some cases, searchable databases to which the analytical methods were applied. The methods of column 7 were used to characterize each polypeptide through sequence
 15 homology and protein motifs.

The columns of Table 3 show the tissue-specificity and diseases, disorders, or conditions associated with nucleotide sequences encoding NuABP. The first column of Table 3 lists the nucleotide SEQ ID NOs. Column 2 lists fragments of the nucleotide sequences of column 1. These fragments are useful, for example, in hybridization or amplification technologies to identify SEQ ID
 20 NO:56-110 and to distinguish between SEQ ID NO:56-110 and related polynucleotide sequences. The polypeptides encoded by these fragments are useful, for example, as immunogenic peptides. Column 3 lists tissue categories which express NuABP as a fraction of total tissues expressing NuABP. Column 4 lists diseases, disorders, or conditions associated with those tissues expressing NuABP as a fraction of total tissues expressing NuABP. Of particular note is the expression of SEQ
 25 ID NO:83 and SEQ ID NO:110 in neurological tissue. About 53% of the cDNA libraries expressing SEQ ID NO:83 are derived from neurological tissue. Furthermore, SEQ ID NO:110 expression is detected exclusively in a cDNA library derived from brain tissue afflicted with Huntington's disease. Column 5 lists the vectors used to subclone each cDNA library.

The columns of Table 4 show descriptions of the tissues used to construct the cDNA libraries
 30 from which cDNA clones encoding NuABP were isolated. Column 1 references the nucleotide SEQ ID NOs, column 2 shows the cDNA libraries from which these clones were isolated, and column 3 shows the tissue origins and other descriptive information relevant to the cDNA libraries in column 2.

Fragments of the nucleotide sequences encoding NuABP are useful, for example, in hybridization or amplification technologies to identify SEQ ID NOS:56-110 and to distinguish
 35 between SEQ ID NOS:56-110 and related polynucleotide sequences. The polypeptides encoded by

these fragments are useful, for example, as immunogenic peptides.

The invention also encompasses NuABP variants. A preferred NuABP variant is one which has at least about 80%, or alternatively at least about 90%, or even at least about 95% amino acid sequence identity to the NuABP amino acid sequence, and which contains at least one functional or structural characteristic of NuABP.

The invention also encompasses polynucleotides which encode NuABP. In a particular embodiment, the invention encompasses a polynucleotide sequence comprising a sequence selected from the group consisting of SEQ ID NO:56-110, which encodes NuABP.

The invention also encompasses a variant of a polynucleotide sequence encoding NuABP. In particular, such a variant polynucleotide sequence will have at least about 70%, or alternatively at least about 85%, or even at least about 95% polynucleotide sequence identity to the polynucleotide sequence encoding NuABP. A particular aspect of the invention encompasses a variant of a polynucleotide sequence comprising a sequence selected from the group consisting of SEQ ID NO:56-110 which has at least about 70%, or alternatively at least about 85%, or even at least about 95% polynucleotide sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:56-110. Any one of the polynucleotide variants described above can encode an amino acid sequence which contains at least one functional or structural characteristic of NuABP.

It will be appreciated by those skilled in the art that as a result of the degeneracy of the genetic code, a multitude of polynucleotide sequences encoding NuABP, some bearing minimal similarity to the polynucleotide sequences of any known and naturally occurring gene, may be produced. Thus, the invention contemplates each and every possible variation of polynucleotide sequence that could be made by selecting combinations based on possible codon choices. These combinations are made in accordance with the standard triplet genetic code as applied to the polynucleotide sequence of naturally occurring NuABP, and all such variations are to be considered as being specifically disclosed.

Although nucleotide sequences which encode NuABP and its variants are generally capable of hybridizing to the nucleotide sequence of the naturally occurring NuABP under appropriately selected conditions of stringency, it may be advantageous to produce nucleotide sequences encoding NuABP or its derivatives possessing a substantially different codon usage, e.g., inclusion of non-naturally occurring codons. Codons may be selected to increase the rate at which expression of the peptide occurs in a particular prokaryotic or eukaryotic host in accordance with the frequency with which particular codons are utilized by the host. Other reasons for substantially altering the nucleotide sequence encoding NuABP and its derivatives without altering the encoded amino acid sequences include the production of RNA transcripts having more desirable properties, such as a greater half-life, than transcripts produced from the naturally occurring sequence.

The invention also encompasses production of DNA sequences which encode NuABP and NuABP derivatives, or fragments thereof, entirely by synthetic chemistry. After production, the synthetic sequence may be inserted into any of the many available expression vectors and cell systems using reagents well known in the art. Moreover, synthetic chemistry may be used to introduce

5 mutations into a sequence encoding NuABP or any fragment thereof.

Also encompassed by the invention are polynucleotide sequences that are capable of hybridizing to the claimed polynucleotide sequences, and, in particular, to those shown in SEQ ID NO:56-110 and fragments thereof under various conditions of stringency. (See, e.g., Wahl, G.M. and S.L. Berger (1987) *Methods Enzymol.* 152:399-407; Kimmel, A.R. (1987) *Methods Enzymol.* 10 152:507-511.) Hybridization conditions, including annealing and wash conditions, are described in "Definitions."

Methods for DNA sequencing are well known in the art and may be used to practice any of the embodiments of the invention. The methods may employ such enzymes as the Klenow fragment of DNA polymerase I, SEQUENASE (US Biochemical, Cleveland OH), Taq polymerase (Perkin-Elmer), thermostable T7 polymerase (Amersham Pharmacia Biotech, Piscataway NJ), or 15 combinations of polymerases and proofreading exonucleases such as those found in the ELONGASE amplification system (Life Technologies, Gaithersburg MD). Preferably, sequence preparation is automated with machines such as the MICROLAB 2200 liquid transfer system (Hamilton, Reno NV), PTC200 thermal cycler (MJ Research, Watertown MA) and ABI CATALYST 800 thermal cycler 20 (Perkin-Elmer). Sequencing is then carried out using either the ABI 373 or 377 DNA sequencing system (Perkin-Elmer), the MEGABACE 1000 DNA sequencing system (Molecular Dynamics, Sunnyvale CA), or other systems known in the art. The resulting sequences are analyzed using a variety of algorithms which are well known in the art. (See, e.g., Ausubel, F.M. (1997) Short Protocols in Molecular Biology, John Wiley & Sons, New York NY, unit 7.7; Meyers, R.A. (1995) 25 Molecular Biology and Biotechnology, Wiley VCH, New York NY, pp. 856-853.)

The nucleic acid sequences encoding NuABP may be extended utilizing a partial nucleotide sequence and employing various PCR-based methods known in the art to detect upstream sequences, such as promoters and regulatory elements. For example, one method which may be employed, restriction-site PCR, uses universal and nested primers to amplify unknown sequence from genomic 30 DNA within a cloning vector. (See, e.g., Sarkar, G. (1993) *PCR Methods Applic.* 2:318-322.) Another method, inverse PCR, uses primers that extend in divergent directions to amplify unknown sequence from a circularized template. The template is derived from restriction fragments comprising a known genomic locus and surrounding sequences. (See, e.g., Triglia, T. et al. (1988) *Nucleic Acids Res.* 16:8186.) A third method, capture PCR, involves PCR amplification of DNA fragments adjacent 35 to known sequences in human and yeast artificial chromosome DNA. (See, e.g., Lagerstrom, M. et al.

(1991) PCR Methods Applic. 1:111-119.) In this method, multiple restriction enzyme digestions and ligations may be used to insert an engineered double-stranded sequence into a region of unknown sequence before performing PCR. Other methods which may be used to retrieve unknown sequences are known in the art. (See, e.g., Parker, J.D. et al. (1991) Nucleic Acids Res. 19:3055-3060).

5 Additionally, one may use PCR, nested primers, and PROMOTERFINDER libraries (Clontech, Palo Alto CA) to walk genomic DNA. This procedure avoids the need to screen libraries and is useful in finding intron/exon junctions. For all PCR-based methods, primers may be designed using commercially available software, such as OLIGO 4.06 Primer Analysis software (National Biosciences, Plymouth MN) or another appropriate program, to be about 22 to 30 nucleotides in

10 length, to have a GC content of about 50% or more, and to anneal to the template at temperatures of about 68°C to 72°C.

When screening for full-length cDNAs, it is preferable to use libraries that have been size-selected to include larger cDNAs. In addition, random-primed libraries, which often include sequences containing the 5' regions of genes, are preferable for situations in which an oligo d(T)

15 library does not yield a full-length cDNA. Genomic libraries may be useful for extension of sequence into 5' non-transcribed regulatory regions.

Capillary electrophoresis systems which are commercially available may be used to analyze the size or confirm the nucleotide sequence of sequencing or PCR products. In particular, capillary sequencing may employ flowable polymers for electrophoretic separation, four different nucleotide-

20 specific, laser-stimulated fluorescent dyes, and a charge coupled device camera for detection of the emitted wavelengths. Output/light intensity may be converted to electrical signal using appropriate software (e.g., GENOTYPER and SEQUENCE NAVIGATOR, Perkin-Elmer), and the entire process from loading of samples to computer analysis and electronic data display may be computer controlled. Capillary electrophoresis is especially preferable for sequencing small DNA fragments which may be

25 present in limited amounts in a particular sample.

In another embodiment of the invention, polynucleotide sequences or fragments thereof which encode NuABP may be cloned in recombinant DNA molecules that direct expression of NuABP, or fragments or functional equivalents thereof, in appropriate host cells. Due to the inherent degeneracy of the genetic code, other DNA sequences which encode substantially the same or a

30 functionally equivalent amino acid sequence may be produced and used to express NuABP.

The nucleotide sequences of the present invention can be engineered using methods generally known in the art in order to alter NuABP-encoding sequences for a variety of purposes including, but not limited to, modification of the cloning, processing, and/or expression of the gene product. DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic

35 oligonucleotides may be used to engineer the nucleotide sequences. For example, oligonucleotide-

mediated site-directed mutagenesis may be used to introduce mutations that create new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, and so forth.

In another embodiment, sequences encoding NuABP may be synthesized, in whole or in part, using chemical methods well known in the art. (See, e.g., Caruthers, M.H. et al. (1980) *Nucleic Acids Symp. Ser.* 7:215-223; and Horn, T. et al. (1980) *Nucleic Acids Symp. Ser.* 7:225-232.)

Alternatively, NuABP itself or a fragment thereof may be synthesized using chemical methods. For example, peptide synthesis can be performed using various solid-phase techniques. (See, e.g., Roberge, J.Y. et al. (1995) *Science* 269:202-204.) Automated synthesis may be achieved using the ABI 431A peptide synthesizer (Perkin-Elmer). Additionally, the amino acid sequence of NuABP, or any part thereof, may be altered during direct synthesis and/or combined with sequences from other proteins, or any part thereof, to produce a variant polypeptide.

The peptide may be substantially purified by preparative high performance liquid chromatography. (See, e.g., Chiez, R.M. and F.Z. Regnier (1990) *Methods Enzymol.* 182:392-421.) The composition of the synthetic peptides may be confirmed by amino acid analysis or by sequencing. (See, e.g., Creighton, T. (1984) Proteins, Structures and Molecular Properties, WH Freeman, New York NY.)

In order to express a biologically active NuABP, the nucleotide sequences encoding NuABP or derivatives thereof may be inserted into an appropriate expression vector, i.e., a vector which contains the necessary elements for transcriptional and translational control of the inserted coding sequence in a suitable host. These elements include regulatory sequences, such as enhancers, constitutive and inducible promoters, and 5' and 3' untranslated regions in the vector and in polynucleotide sequences encoding NuABP. Such elements may vary in their strength and specificity. Specific initiation signals may also be used to achieve more efficient translation of sequences encoding NuABP. Such signals include the ATG initiation codon and adjacent sequences, e.g. the Kozak sequence. In cases where sequences encoding NuABP and its initiation codon and upstream regulatory sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a fragment thereof, is inserted, exogenous translational control signals including an in-frame ATG initiation codon should be provided by the vector. Exogenous translational elements and initiation codons may be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers appropriate for the particular host cell system used. (See, e.g., Scharf, D. et al. (1994) *Results Probl. Cell Differ.* 20:125-162.)

Methods which are well known to those skilled in the art may be used to construct expression vectors containing sequences encoding NuABP and appropriate transcriptional and translational control elements. These methods include in vitro recombinant DNA techniques, synthetic techniques,

and in vivo genetic recombination. (See, e.g., Sambrook, J. et al. (1989) Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Press, Plainview NY, ch. 4, 8, and 16-17; Ausubel, F.M. et al. (1995) Current Protocols in Molecular Biology, John Wiley & Sons, New York NY, ch. 9, 13, and 16.)

5 A variety of expression vector/host systems may be utilized to contain and express sequences encoding NuABP. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with viral expression vectors (e.g., baculovirus); plant cell systems transformed with viral expression vectors (e.g., cauliflower mosaic virus, CaMV, or tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids); or
10 animal cell systems. The invention is not limited by the host cell employed.

In bacterial systems, a number of cloning and expression vectors may be selected depending upon the use intended for polynucleotide sequences encoding NuABP. For example, routine cloning, subcloning, and propagation of polynucleotide sequences encoding NuABP can be achieved using a
15 multifunctional E. coli vector such as PBLUESCRIPT (Stratagene, La Jolla CA) or PSORT1 plasmid (Life Technologies). Ligation of sequences encoding NuABP into the vector's multiple cloning site disrupts the *lacZ* gene, allowing a colorimetric screening procedure for identification of transformed bacteria containing recombinant molecules. In addition, these vectors may be useful for in vitro transcription, dideoxy sequencing, single strand rescue with helper phage, and creation of
20 nested deletions in the cloned sequence. (See, e.g., Van Heeke, G. and S.M. Schuster (1989) J. Biol. Chem. 264:5503-5509.) When large quantities of NuABP are needed, e.g. for the production of antibodies, vectors which direct high level expression of NuABP may be used. For example, vectors containing the strong, inducible T5 or T7 bacteriophage promoter may be used.

Yeast expression systems may be used for production of NuABP. A number of vectors
25 containing constitutive or inducible promoters, such as alpha factor, alcohol oxidase, and PGH promoters, may be used in the yeast Saccharomyces cerevisiae or Pichia pastoris. In addition, such vectors direct either the secretion or intracellular retention of expressed proteins and enable integration of foreign sequences into the host genome for stable propagation. (See, e.g., Ausubel, 1995, supra; Bitter, G.A. et al. (1987) Methods Enzymol. 153:516-544; and Scorer, C.A. et al. (1994)
30 Bio/Technology 12:181-184.)

Plant systems may also be used for expression of NuABP. Transcription of sequences encoding NuABP may be driven viral promoters, e.g., the 35S and 19S promoters of CaMV used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) EMBO J. 6:307-311). Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock
35 promoters may be used. (See, e.g., Coruzzi, G. et al. (1984) EMBO J. 3:1671-1680; Broglie, R. et al.

(1984) Science 224:838-843; and Winter, J. et al. (1991) Results Probl. Cell Differ. 17:85-105.)

These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. (See, e.g., The McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York NY, pp. 191-196.)

5 In mammalian cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, sequences encoding NuABP may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain infective virus which expresses NuABP in host cells. (See, e.g., Logan, J. and T. Shenk (1984) Proc.
10 Natl. Acad. Sci. USA 81:3655-3659.) In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells. SV40 or EBV-based vectors may also be used for high-level protein expression.

Human artificial chromosomes (HACs) may also be employed to deliver larger fragments of DNA than can be contained in and expressed from a plasmid. HACs of about 6 kb to 10 Mb are
15 constructed and delivered via conventional delivery methods (liposomes, polycationic amino polymers, or vesicles) for therapeutic purposes. (See, e.g., Harrington, J.J. et al. (1997) Nat. Genet. 15:345-355.)

For long term production of recombinant proteins in mammalian systems, stable expression of NuABP in cell lines is preferred. For example, sequences encoding NuABP can be transformed into
20 cell lines using expression vectors which may contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells may be allowed to grow for about 1 to 2 days in enriched media before being switched to selective media. The purpose of the selectable marker is to confer resistance to a selective agent, and its presence allows growth and recovery of cells which successfully express
25 the introduced sequences. Resistant clones of stably transformed cells may be propagated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase and adenine phosphoribosyltransferase genes, for use in *tk*⁻ and *apr*⁻ cells, respectively. (See, e.g., Wigler, M. et
30 al. (1977) Cell 11:223-232; Lowy, I. et al. (1980) Cell 22:817-823.) Also, antimetabolite, antibiotic, or herbicide resistance can be used as the basis for selection. For example, *dhfr* confers resistance to methotrexate; *neo* confers resistance to the aminoglycosides neomycin and G-418; and *als* and *pat* confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively. (See, e.g.,
Wigler, M. et al. (1980) Proc. Natl. Acad. Sci. USA 77:3567-3570; Colbere-Garapin, F. et al. (1981)
35 J. Mol. Biol. 150:1-14.) Additional selectable genes have been described, e.g., *trpB* and *hisD*, which

alter cellular requirements for metabolites. (See, e.g., Hartman, S.C. and R.C. Mulligan (1988) Proc. Natl. Acad. Sci. USA 85:8047-8051.) Visible markers, e.g., anthocyanins, green fluorescent proteins (GFP: Clontech), β glucuronidase and its substrate β -glucuronide, or luciferase and its substrate luciferin may be used. These markers can be used not only to identify transformants, but also to
5 quantify the amount of transient or stable protein expression attributable to a specific vector system. (See, e.g., Rhodes, C.A. (1995) Methods Mol. Biol. 55:121-131.)

Although the presence/absence of marker gene expression suggests that the gene of interest is also present, the presence and expression of the gene may need to be confirmed. For example, if the sequence encoding NuABP is inserted within a marker gene sequence, transformed cells containing
10 sequences encoding NuABP can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a sequence encoding NuABP under the control of a single promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

In general, host cells that contain the nucleic acid sequence encoding NuABP and that express
15 NuABP may be identified by a variety of procedures known to those of skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridizations, PCR amplification, and protein bioassay or immunoassay techniques which include membrane, solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein sequences.

Immunological methods for detecting and measuring the expression of NuABP using either
20 specific polyclonal or monoclonal antibodies are known in the art. Examples of such techniques include enzyme-linked immunosorbent assays (ELISAs), radioimmunoassays (RIAs), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on NuABP is preferred, but a competitive binding assay may be employed. These and other assays are well known in the art. (See,
25 e.g., Hampton, R. et al. (1990) Serological Methods, a Laboratory Manual, APS Press, St. Paul MN, Sect. IV; Coligan, J.E. et al. (1997) Current Protocols in Immunology, Greene Pub. Associates and Wiley-Interscience, New York NY; and Pound, J.D. (1998) Immunochemical Protocols, Humana Press, Totowa NJ.)

A wide variety of labels and conjugation techniques are known by those skilled in the art and
30 may be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides encoding NuABP include oligolabeling, nick translation, end-labeling, or PCR amplification using a labeled nucleotide. Alternatively, the sequences encoding NuABP, or any fragments thereof, may be cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are commercially available,
35 and may be used to synthesize RNA probes in vitro by addition of an appropriate RNA polymerase

such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits, such as those provided by Amersham Pharmacia Biotech, Promega (Madison WI), and US Biochemical. Suitable reporter molecules or labels which may be used for ease of detection include radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents, as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

Host cells transformed with nucleotide sequences encoding NuABP may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a transformed cell may be secreted or retained intracellularly depending on the sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing polynucleotides which encode NuABP may be designed to contain signal sequences which direct secretion of NuABP through a prokaryotic or eukaryotic cell membrane.

In addition, a host cell strain may be chosen for its ability to modulate expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing which cleaves a "prepro" or "pro" form of the protein may also be used to specify protein targeting, folding, and/or activity. Different host cells which have specific cellular machinery and characteristic mechanisms for post-translational activities (e.g., CHO, HeLa, MDCK, HEK293, and WI38) are available from the American Type Culture Collection (ATCC, Manassas VA) and may be chosen to ensure the correct modification and processing of the foreign protein.

In another embodiment of the invention, natural, modified, or recombinant nucleic acid sequences encoding NuABP may be ligated to a heterologous sequence resulting in translation of a fusion protein in any of the aforementioned host systems. For example, a chimeric NuABP protein containing a heterologous moiety that can be recognized by a commercially available antibody may facilitate the screening of peptide libraries for inhibitors of NuABP activity. Heterologous protein and peptide moieties may also facilitate purification of fusion proteins using commercially available affinity matrices. Such moieties include, but are not limited to, glutathione S-transferase (GST), maltose binding protein (MBP), thioredoxin (Trx), calmodulin binding peptide (CBP), 6-His, FLAG, *c-myc*, and hemagglutinin (HA). GST, MBP, Trx, CBP, and 6-His enable purification of their cognate fusion proteins on immobilized glutathione, maltose, phenylarsine oxide, calmodulin, and metal-chelate resins, respectively. FLAG, *c-myc*, and hemagglutinin (HA) enable immunoaffinity purification of fusion proteins using commercially available monoclonal and polyclonal antibodies that specifically recognize these epitope tags. A fusion protein may also be engineered to contain a proteolytic cleavage site located between the NuABP encoding sequence and the heterologous protein sequence, so that NuABP may be cleaved away from the heterologous moiety following purification.

Methods for fusion protein expression and purification are discussed in Ausubel (1995, supra, ch. 10). A variety of commercially available kits may also be used to facilitate expression and purification of fusion proteins.

In a further embodiment of the invention, synthesis of radiolabeled NuABP may be achieved
5 in vitro using the TNT rabbit reticulocyte lysate or wheat germ extract system (Promega). These systems couple transcription and translation of protein-coding sequences operably associated with the T7, T3, or SP6 promoters. Translation takes place in the presence of a radiolabeled amino acid precursor, for example, ³⁵S-methionine.

Fragments of NuABP may be produced not only by recombinant means, but also by direct
10 peptide synthesis using solid-phase techniques. (See, e.g., Creighton, supra, pp. 55-60.) Protein synthesis may be performed by manual techniques or by automation. Automated synthesis may be achieved, for example, using the ABI 431A peptide synthesizer (Perkin-Elmer). Various fragments of NuABP may be synthesized separately and then combined to produce the full length molecule.

THERAPEUTICS

15 Chemical and structural similarity, e.g., in the context of sequences and motifs, exists between regions of NuABP and nucleic-acid binding proteins. In addition, the expression of NuABP is closely associated with proliferative, neuronal, inflamed, and cancerous tissues and tissues of the reproductive system. Therefore, NuABP appears to play a role in reproductive, immune, and neurological disorders, and cell proliferative disorders including cancer. In the treatment of disorders associated
20 with increased NuABP expression or activity, it is desirable to decrease the expression or activity of NuABP. In the treatment of disorders associated with decreased NuABP expression or activity, it is desirable to increase the expression or activity of NuABP.

Therefore, in one embodiment, NuABP or a fragment or derivative thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity
25 of NuABP. Examples of such disorders include, but are not limited to, a reproductive disorder such as disorders of prolactin production, infertility, including tubal disease, ovulatory defects, and endometriosis, disruptions of the estrous cycle, disruptions of the menstrual cycle, polycystic ovary syndrome, ovarian hyperstimulation syndrome, endometrial and ovarian tumors, uterine fibroids, autoimmune disorders, ectopic pregnancies, and teratogenesis; cancer of the breast, fibrocystic breast
30 disease, and galactorrhea; disruptions of spermatogenesis, abnormal sperm physiology, cancer of the testis, cancer of the prostate, benign prostatic hyperplasia, prostatitis, Peyronie's disease, impotence, carcinoma of the male breast, and gynecomastia; an immune disorder such as inflammation, actinic keratosis, acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, arteriosclerosis, asthma,
35 atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, bronchitis, bursitis,

cholecystitis, cirrhosis, contact dermatitis, Crohn's disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Graves' disease, Hashimoto's thyroiditis, paroxysmal nocturnal hemoglobinuria, hepatitis, hypereosinophilia, irritable bowel syndrome,

5 episodic lymphopenia with lymphocytotoxins, mixed connective tissue disease (MCTD), multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, myelofibrosis, osteoarthritis, osteoporosis, pancreatitis, polycythemia vera, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic anaphylaxis, systemic lupus erythematosus, systemic sclerosis, primary thrombocythemia, thrombocytopenic purpura, ulcerative colitis, uveitis,

10 Werner syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, trauma, and hematopoietic cancer including lymphoma, leukemia, and myeloma; a neurological disorder such as epilepsy, ischemic cerebrovascular disease, stroke, cerebral neoplasms, Alzheimer's disease, Pick's disease, Huntington's disease, dementia, Parkinson's disease and other extrapyramidal disorders, amyotrophic lateral sclerosis and other motor neuron disorders, progressive neural muscular atrophy,

15 retinitis pigmentosa, hereditary ataxias, multiple sclerosis and other demyelinating diseases, bacterial and viral meningitis, brain abscess, subdural empyema, epidural abscess, suppurative intracranial thrombophlebitis, myelitis and radiculitis, viral central nervous system disease, prion diseases including kuru, Creutzfeldt-Jakob disease, and Gerstmann-Straussler-Scheinker syndrome, fatal familial insomnia, nutritional and metabolic diseases of the nervous system, neurofibromatosis,

20 tuberous sclerosis, cerebelloretinal hemangioblastomatosis, encephalotrigeminal syndrome, mental retardation and other developmental disorders of the central nervous system, cerebral palsy, neuroskeletal disorders, autonomic nervous system disorders, cranial nerve disorders, spinal cord diseases, muscular dystrophy and other neuromuscular disorders, peripheral nervous system disorders, dermatomyositis and polymyositis, inherited, metabolic, endocrine, and toxic myopathies,

25 myasthenia gravis, periodic paralysis, mental disorders including mood, anxiety, and schizophrenic disorders, akathisia, amnesia, catatonia, diabetic neuropathy, tardive dyskinesia, dystonias, paranoid psychoses, postherpetic neuralgia, and Tourette's disorder; and a cell proliferative disorder such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, mixed connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnal hemoglobinuria, polycythemia vera, psoriasis,

30 primary thrombocythemia, and cancers including adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus.

35 In another embodiment, a vector capable of expressing NuABP or a fragment or derivative

thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of NuABP including, but not limited to, those described above.

In a further embodiment, a pharmaceutical composition comprising a substantially purified NuABP in conjunction with a suitable pharmaceutical carrier may be administered to a subject to treat
5 or prevent a disorder associated with decreased expression or activity of NuABP including, but not limited to, those provided above.

In still another embodiment, an agonist which modulates the activity of NuABP may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of NuABP including, but not limited to, those listed above.

10 In a further embodiment, an antagonist of NuABP may be administered to a subject to treat or prevent a disorder associated with increased expression or activity of NuABP. Examples of such disorders include, but are not limited to, those reproductive, immune, and neurological disorders, and cell proliferative disorders including cancer, described above. In one aspect, an antibody which specifically binds NuABP may be used directly as an antagonist or indirectly as a targeting or delivery
15 mechanism for bringing a pharmaceutical agent to cells or tissues which express NuABP.

In an additional embodiment, a vector expressing the complement of the polynucleotide encoding NuABP may be administered to a subject to treat or prevent a disorder associated with increased expression or activity of NuABP including, but not limited to, those described above.

In other embodiments, any of the proteins, antagonists, antibodies, agonists, complementary
20 sequences, or vectors of the invention may be administered in combination with other appropriate therapeutic agents. Selection of the appropriate agents for use in combination therapy may be made by one of ordinary skill in the art, according to conventional pharmaceutical principles. The combination of therapeutic agents may act synergistically to effect the treatment or prevention of the various disorders described above. Using this approach, one may be able to achieve therapeutic
25 efficacy with lower dosages of each agent, thus reducing the potential for adverse side effects.

An antagonist of NuABP may be produced using methods which are generally known in the art. In particular, purified NuABP may be used to produce antibodies or to screen libraries of pharmaceutical agents to identify those which specifically bind NuABP. Antibodies to NuABP may also be generated using methods that are well known in the art. Such antibodies may include, but are
30 not limited to, polyclonal, monoclonal, chimeric, and single chain antibodies, Fab fragments, and fragments produced by a Fab expression library. Neutralizing antibodies (i.e., those which inhibit dimer formation) are generally preferred for therapeutic use.

For the production of antibodies, various hosts including goats, rabbits, rats, mice, humans, and others may be immunized by injection with NuABP or with any fragment or oligopeptide thereof
35 which has immunogenic properties. Depending on the host species, various adjuvants may be used to

increase immunological response. Such adjuvants include, but are not limited to, Freund's, mineral gels such as aluminum hydroxide, and surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, KLH, and dinitrophenol. Among adjuvants used in humans, BCG (bacilli Calmette-Guerin) and Corynebacterium parvum are especially preferable.

5 It is preferred that the oligopeptides, peptides, or fragments used to induce antibodies to NuABP have an amino acid sequence consisting of at least about 5 amino acids, and generally will consist of at least about 10 amino acids. It is also preferable that these oligopeptides, peptides, or fragments are identical to a portion of the amino acid sequence of the natural protein and contain the entire amino acid sequence of a small, naturally occurring molecule. Short stretches of NuABP amino
10 acids may be fused with those of another protein, such as KLH, and antibodies to the chimeric molecule may be produced.

Monoclonal antibodies to NuABP may be prepared using any technique which provides for the production of antibody molecules by continuous cell lines in culture. These include, but are not limited to, the hybridoma technique, the human B-cell hybridoma technique, and the EBV-hybridoma
15 technique. (See, e.g., Kohler, G. et al. (1975) Nature 256:495-497; Kozbor, D. et al. (1985) J. Immunol. Methods 81:31-42; Cote, R.J. et al. (1983) Proc. Natl. Acad. Sci. USA 80:2026-2030; and Cole, S.P. et al. (1984) Mol. Cell Biol. 62:109-120.)

In addition, techniques developed for the production of "chimeric antibodies," such as the splicing of mouse antibody genes to human antibody genes to obtain a molecule with appropriate
20 antigen specificity and biological activity, can be used. (See, e.g., Morrison, S.L. et al. (1984) Proc. Natl. Acad. Sci. USA 81:6851-6855; Neuberger, M.S. et al. (1984) Nature 312:604-608; and Takeda, S. et al. (1985) Nature 314:452-454.) Alternatively, techniques described for the production of single chain antibodies may be adapted, using methods known in the art, to produce NuABP-specific single chain antibodies. Antibodies with related specificity, but of distinct idiotypic composition, may be
25 generated by chain shuffling from random combinatorial immunoglobulin libraries. (See, e.g., Burton, D.R. (1991) Proc. Natl. Acad. Sci. USA 88:10134-10137.)

Antibodies may also be produced by inducing in vivo production in the lymphocyte population or by screening immunoglobulin libraries or panels of highly specific binding reagents as disclosed in the literature. (See, e.g., Orlandi, R. et al. (1989) Proc. Natl. Acad. Sci. USA
30 86:3833-3837; Winter, G. et al. (1991) Nature 349:293-299.)

Antibody fragments which contain specific binding sites for NuABP may also be generated. For example, such fragments include, but are not limited to, F(ab')₂ fragments produced by pepsin digestion of the antibody molecule and Fab fragments generated by reducing the disulfide bridges of the F(ab')₂ fragments. Alternatively, Fab expression libraries may be constructed to allow rapid and
35 easy identification of monoclonal Fab fragments with the desired specificity. (See, e.g., Huse, W.D.

et al. (1989) Science 246:1275-1281.)

Various immunoassays may be used for screening to identify antibodies having the desired specificity. Numerous protocols for competitive binding or immunoradiometric assays using either polyclonal or monoclonal antibodies with established specificities are well known in the art. Such immunoassays typically involve the measurement of complex formation between NuABP and its specific antibody. A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering NuABP epitopes is generally used, but a competitive binding assay may also be employed (Pound, supra).

Various methods such as Scatchard analysis in conjunction with radioimmunoassay techniques may be used to assess the affinity of antibodies for NuABP. Affinity is expressed as an association constant, K_a , which is defined as the molar concentration of NuABP-antibody complex divided by the molar concentrations of free antigen and free antibody under equilibrium conditions. The K_a determined for a preparation of polyclonal antibodies, which are heterogeneous in their affinities for multiple NuABP epitopes, represents the average affinity, or avidity, of the antibodies for NuABP. The K_a determined for a preparation of monoclonal antibodies, which are monospecific for a particular NuABP epitope, represents a true measure of affinity. High-affinity antibody preparations with K_a ranging from about 10^9 to 10^{12} L/mole are preferred for use in immunoassays in which the NuABP-antibody complex must withstand rigorous manipulations. Low-affinity antibody preparations with K_a ranging from about 10^6 to 10^7 L/mole are preferred for use in immunopurification and similar procedures which ultimately require dissociation of NuABP, preferably in active form, from the antibody (Catty, D. (1988) Antibodies. Volume I: A Practical Approach, IRL Press, Washington, DC; Liddell, J.E. and Cryer, A. (1991) A Practical Guide to Monoclonal Antibodies, John Wiley & Sons, New York NY).

The titer and avidity of polyclonal antibody preparations may be further evaluated to determine the quality and suitability of such preparations for certain downstream applications. For example, a polyclonal antibody preparation containing at least 1-2 mg specific antibody/ml, preferably 5-10 mg specific antibody/ml, is generally employed in procedures requiring precipitation of NuABP-antibody complexes. Procedures for evaluating antibody specificity, titer, and avidity, and guidelines for antibody quality and usage in various applications, are generally available. (See, e.g., Catty, supra, and Coligan et al. supra.)

In another embodiment of the invention, the polynucleotides encoding NuABP, or any fragment or complement thereof, may be used for therapeutic purposes. In one aspect, the complement of the polynucleotide encoding NuABP may be used in situations in which it would be desirable to block the transcription of the mRNA. In particular, cells may be transformed with sequences complementary to polynucleotides encoding NuABP. Thus, complementary molecules or

fragments may be used to modulate NuABP activity, or to achieve regulation of gene function. Such technology is now well known in the art, and sense or antisense oligonucleotides or larger fragments can be designed from various locations along the coding or control regions of sequences encoding NuABP.

5 Expression vectors derived from retroviruses, adenoviruses, or herpes or vaccinia viruses, or from various bacterial plasmids, may be used for delivery of nucleotide sequences to the targeted organ, tissue, or cell population. Methods which are well known to those skilled in the art can be used to construct vectors to express nucleic acid sequences complementary to the polynucleotides encoding NuABP. (See, e.g., Sambrook, supra; Ausubel, 1995, supra.)

10 Genes encoding NuABP can be turned off by transforming a cell or tissue with expression vectors which express high levels of a polynucleotide, or fragment thereof, encoding NuABP. Such constructs may be used to introduce untranslatable sense or antisense sequences into a cell. Even in the absence of integration into the DNA, such vectors may continue to transcribe RNA molecules until they are disabled by endogenous nucleases. Transient expression may last for a month or more
15 with a non-replicating vector, and may last even longer if appropriate replication elements are part of the vector system.

As mentioned above, modifications of gene expression can be obtained by designing complementary sequences or antisense molecules (DNA, RNA, or PNA) to the control, 5', or regulatory regions of the gene encoding NuABP. Oligonucleotides derived from the transcription
20 initiation site, e.g., between about positions -10 and +10 from the start site, may be employed. Similarly, inhibition can be achieved using triple helix base-pairing methodology. Triple helix pairing is useful because it causes inhibition of the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors, or regulatory molecules. Recent therapeutic advances using triplex DNA have been described in the literature. (See, e.g., Gee, J.E. et al. (1994) in Huber,
25 B.E. and B.I. Carr, Molecular and Immunologic Approaches, Futura Publishing, Mt. Kisco NY, pp. 163-177.) A complementary sequence or antisense molecule may also be designed to block translation of mRNA by preventing the transcript from binding to ribosomes.

Ribozymes, enzymatic RNA molecules, may also be used to catalyze the specific cleavage of RNA. The mechanism of ribozyme action involves sequence-specific hybridization of the ribozyme
30 molecule to complementary target RNA, followed by endonucleolytic cleavage. For example, engineered hammerhead motif ribozyme molecules may specifically and efficiently catalyze endonucleolytic cleavage of sequences encoding NuABP.

Specific ribozyme cleavage sites within any potential RNA target are initially identified by scanning the target molecule for ribozyme cleavage sites, including the following sequences: GUA,
35 GUU, and GUC. Once identified, short RNA sequences of between 15 and 20 ribonucleotides,

corresponding to the region of the target gene containing the cleavage site, may be evaluated for secondary structural features which may render the oligonucleotide inoperable. The suitability of candidate targets may also be evaluated by testing accessibility to hybridization with complementary oligonucleotides using ribonuclease protection assays.

5 Complementary ribonucleic acid molecules and ribozymes of the invention may be prepared by any method known in the art for the synthesis of nucleic acid molecules. These include techniques for chemically synthesizing oligonucleotides such as solid phase phosphoramidite chemical synthesis. Alternatively, RNA molecules may be generated by in vitro and in vivo transcription of DNA sequences encoding NuABP. Such DNA sequences may be incorporated into a wide variety of
10 vectors with suitable RNA polymerase promoters such as T7 or SP6. Alternatively, these cDNA constructs that synthesize complementary RNA, constitutively or inducibly, can be introduced into cell lines, cells, or tissues.

RNA molecules may be modified to increase intracellular stability and half-life. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends
15 of the molecule, or the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages within the backbone of the molecule. This concept is inherent in the production of PNAs and can be extended in all of these molecules by the inclusion of nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, cytidine, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.

20 Many methods for introducing vectors into cells or tissues are available and equally suitable for use in vivo, in vitro, and ex vivo. For ex vivo therapy, vectors may be introduced into stem cells taken from the patient and clonally propagated for autologous transplant back into that same patient. Delivery by transfection, by liposome injections, or by polycationic amino polymers may be achieved using methods which are well known in the art. (See, e.g., Goldman, C.K. et al. (1997) Nat.
25 Biotechnol. 15:462-466.)

Any of the therapeutic methods described above may be applied to any subject in need of such therapy, including, for example, mammals such as humans, dogs, cats, cows, horses, rabbits, and monkeys.

An additional embodiment of the invention relates to the administration of a pharmaceutical
30 or sterile composition, in conjunction with a pharmaceutically acceptable carrier, for any of the therapeutic effects discussed above. Such pharmaceutical compositions may consist of NuABP, antibodies to NuABP, and mimetics, agonists, antagonists, or inhibitors of NuABP. The compositions may be administered alone or in combination with at least one other agent, such as a stabilizing compound, which may be administered in any sterile, biocompatible pharmaceutical carrier including,
35 but not limited to, saline, buffered saline, dextrose, and water. The compositions may be administered

to a patient alone, or in combination with other agents, drugs, or hormones.

The pharmaceutical compositions utilized in this invention may be administered by any number of routes including, but not limited to, oral, intravenous, intramuscular, intra-arterial, intramedullary, intrathecal, intraventricular, transdermal, subcutaneous, intraperitoneal, intranasal, enteral, topical, sublingual, or rectal means.

In addition to the active ingredients, these pharmaceutical compositions may contain suitable pharmaceutically-acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. Further details on techniques for formulation and administration may be found in the latest edition of Remington's
10 Pharmaceutical Sciences (Maack Publishing, Easton PA).

Pharmaceutical compositions for oral administration can be formulated using pharmaceutically acceptable carriers well known in the art in dosages suitable for oral administration. Such carriers enable the pharmaceutical compositions to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions, and the like, for ingestion by the patient.

15 Pharmaceutical preparations for oral use can be obtained through combining active compounds with solid excipient and processing the resultant mixture of granules (optionally, after grinding) to obtain tablets or dragee cores. Suitable auxiliaries can be added, if desired. Suitable excipients include carbohydrate or protein fillers, such as sugars, including lactose, sucrose, mannitol, and sorbitol; starch from corn, wheat, rice, potato, or other plants; cellulose, such as methyl cellulose,
20 hydroxypropylmethyl-cellulose, or sodium carboxymethylcellulose; gums, including arabic and tragacanth; and proteins, such as gelatin and collagen. If desired, disintegrating or solubilizing agents may be added, such as the cross-linked polyvinyl pyrrolidone, agar, and alginic acid or a salt thereof, such as sodium alginate.

Dragee cores may be used in conjunction with suitable coatings, such as concentrated sugar
25 solutions, which may also contain gum arabic, talc, polyvinylpyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for product identification or to characterize the quantity of active compound, i.e., dosage.

Pharmaceutical preparations which can be used orally include push-fit capsules made of
30 gelatin, as well as soft, sealed capsules made of gelatin and a coating, such as glycerol or sorbitol. Push-fit capsules can contain active ingredients mixed with fillers or binders, such as lactose or starches, lubricants, such as talc or magnesium stearate, and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid, or liquid polyethylene glycol with or without stabilizers.

35 Pharmaceutical formulations suitable for parenteral administration may be formulated in

aqueous solutions, preferably in physiologically compatible buffers such as Hanks' solution, Ringer's solution, or physiologically buffered saline. Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Additionally, suspensions of the active compounds may be prepared as appropriate oily
5 injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils, such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate, triglycerides, or liposomes. Non-lipid polycationic amino polymers may also be used for delivery. Optionally, the suspension may also contain suitable stabilizers or agents to increase the solubility of the compounds and allow for the preparation of highly concentrated solutions.

10 For topical or nasal administration, penetrants appropriate to the particular barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

The pharmaceutical compositions of the present invention may be manufactured in a manner that is known in the art, e.g., by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping, or lyophilizing processes.

15 The pharmaceutical composition may be provided as a salt and can be formed with many acids, including but not limited to, hydrochloric, sulfuric, acetic, lactic, tartaric, malic, and succinic acids. Salts tend to be more soluble in aqueous or other protonic solvents than are the corresponding free base forms. In other cases, the preparation may be a lyophilized powder which may contain any or all of the following: 1 mM to 50 mM histidine, 0.1% to 2% sucrose, and 2% to 7% mannitol, at a
20 pH range of 4.5 to 5.5, that is combined with buffer prior to use.

After pharmaceutical compositions have been prepared, they can be placed in an appropriate container and labeled for treatment of an indicated condition. For administration of NuABP, such labeling would include amount, frequency, and method of administration.

25 Pharmaceutical compositions suitable for use in the invention include compositions wherein the active ingredients are contained in an effective amount to achieve the intended purpose. The determination of an effective dose is well within the capability of those skilled in the art.

For any compound, the therapeutically effective dose can be estimated initially either in cell culture assays, e.g., of neoplastic cells, or in animal models such as mice, rats, rabbits, dogs, or pigs. An animal model may also be used to determine the appropriate concentration range and route of
30 administration. Such information can then be used to determine useful doses and routes for administration in humans.

A therapeutically effective dose refers to that amount of active ingredient, for example NuABP or fragments thereof, antibodies of NuABP, and agonists, antagonists or inhibitors of NuABP, which ameliorates the symptoms or condition. Therapeutic efficacy and toxicity may be
35 determined by standard pharmaceutical procedures in cell cultures or with experimental animals, such

as by calculating the ED_{50} (the dose therapeutically effective in 50% of the population) or LD_{50} (the dose lethal to 50% of the population) statistics. The dose ratio of toxic to therapeutic effects is the therapeutic index, which can be expressed as the LD_{50}/ED_{50} ratio. Pharmaceutical compositions which exhibit large therapeutic indices are preferred. The data obtained from cell culture assays and animal studies are used to formulate a range of dosage for human use. The dosage contained in such compositions is preferably within a range of circulating concentrations that includes the ED_{50} with little or no toxicity. The dosage varies within this range depending upon the dosage form employed, the sensitivity of the patient, and the route of administration.

The exact dosage will be determined by the practitioner, in light of factors related to the subject requiring treatment. Dosage and administration are adjusted to provide sufficient levels of the active moiety or to maintain the desired effect. Factors which may be taken into account include the severity of the disease state, the general health of the subject, the age, weight, and gender of the subject, time and frequency of administration, drug combination(s), reaction sensitivities, and response to therapy. Long-acting pharmaceutical compositions may be administered every 3 to 4 days, every week, or biweekly depending on the half-life and clearance rate of the particular formulation.

Normal dosage amounts may vary from about 0.1 μg to 100,000 μg , up to a total dose of about 1 gram, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature and generally available to practitioners in the art.

Those skilled in the art will employ different formulations for nucleotides than for proteins or their inhibitors. Similarly, delivery of polynucleotides or polypeptides will be specific to particular cells, conditions, locations, etc.

DIAGNOSTICS

In another embodiment, antibodies which specifically bind NuABP may be used for the diagnosis of disorders characterized by expression of NuABP, or in assays to monitor patients being treated with NuABP or agonists, antagonists, or inhibitors of NuABP. Antibodies useful for diagnostic purposes may be prepared in the same manner as described above for therapeutics.

Diagnostic assays for NuABP include methods which utilize the antibody and a label to detect NuABP in human body fluids or in extracts of cells or tissues. The antibodies may be used with or without modification, and may be labeled by covalent or non-covalent attachment of a reporter molecule. A wide variety of reporter molecules, several of which are described above, are known in the art and may be used.

A variety of protocols for measuring NuABP, including ELISAs, RIAs, and FACS, are known in the art and provide a basis for diagnosing altered or abnormal levels of NuABP expression.

Normal or standard values for NuABP expression are established by combining body fluids or cell

extracts taken from normal mammalian subjects, for example, human subjects, with antibody to NuABP under conditions suitable for complex formation. The amount of standard complex formation may be quantitated by various methods, such as photometric means. Quantities of NuABP expressed in subject, control, and disease samples from biopsied tissues are compared with the standard values.

- 5 Deviation between standard and subject values establishes the parameters for diagnosing disease.

In another embodiment of the invention, the polynucleotides encoding NuABP may be used for diagnostic purposes. The polynucleotides which may be used include oligonucleotide sequences, complementary RNA and DNA molecules, and PNAs. The polynucleotides may be used to detect and quantify gene expression in biopsied tissues in which expression of NuABP may be correlated with disease. The diagnostic assay may be used to determine absence, presence, and excess expression of NuABP, and to monitor regulation of NuABP levels during therapeutic intervention.

In one aspect, hybridization with PCR probes which are capable of detecting polynucleotide sequences, including genomic sequences, encoding NuABP or closely related molecules may be used to identify nucleic acid sequences which encode NuABP. The specificity of the probe, whether it is made from a highly specific region, e.g., the 5' regulatory region, or from a less specific region, e.g., a conserved motif, and the stringency of the hybridization or amplification will determine whether the probe identifies only naturally occurring sequences encoding NuABP, allelic variants, or related sequences.

Probes may also be used for the detection of related sequences, and may have at least 50% sequence identity to any of the NuABP encoding sequences. The hybridization probes of the subject invention may be DNA or RNA and may be derived from the sequence of SEQ ID NO:56-110 or from genomic sequences including promoters, enhancers, and introns of the NuABP gene.

Means for producing specific hybridization probes for DNAs encoding NuABP include the cloning of polynucleotide sequences encoding NuABP or NuABP derivatives into vectors for the production of mRNA probes. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro by means of the addition of the appropriate RNA polymerases and the appropriate labeled nucleotides. Hybridization probes may be labeled by a variety of reporter groups, for example, by radionuclides such as ^{32}P or ^{35}S , or by enzymatic labels, such as alkaline phosphatase coupled to the probe via avidin/biotin coupling systems, and the like.

Polynucleotide sequences encoding NuABP may be used for the diagnosis of disorders associated with expression of NuABP. Examples of such disorders include, but are not limited to, a reproductive disorder such as disorders of prolactin production, infertility, including tubal disease, ovulatory defects, and endometriosis, disruptions of the estrous cycle, disruptions of the menstrual cycle, polycystic ovary syndrome, ovarian hyperstimulation syndrome, endometrial and ovarian tumors, uterine fibroids, autoimmune disorders, ectopic pregnancies, and teratogenesis; cancer of the

breast, fibrocystic breast disease, and galactorrhea; disruptions of spermatogenesis, abnormal sperm physiology, cancer of the testis, cancer of the prostate, benign prostatic hyperplasia, prostatitis, Peyronie's disease, impotence, carcinoma of the male breast, and gynecomastia; an immune disorder such as inflammation, actinic keratosis, acquired immunodeficiency syndrome (AIDS), Addison's

5 disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, arteriosclerosis, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, bronchitis, bursitis, cholecystitis, cirrhosis, contact dermatitis, Crohn's disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Graves' disease, Hashimoto's

10 thyroiditis, paroxysmal nocturnal hemoglobinuria, hepatitis, hypereosinophilia, irritable bowel syndrome, episodic lymphopenia with lymphocytotoxins, mixed connective tissue disease (MCTD), multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, myelofibrosis, osteoarthritis, osteoporosis, pancreatitis, polycythemia vera, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic anaphylaxis, systemic

15 lupus erythematosus, systemic sclerosis, primary thrombocythemia, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, trauma, and hematopoietic cancer including lymphoma, leukemia, and myeloma; a neurological disorder such as epilepsy, ischemic cerebrovascular disease, stroke, cerebral neoplasms, Alzheimer's disease, Pick's disease, Huntington's disease, dementia, Parkinson's disease

20 and other extrapyramidal disorders, amyotrophic lateral sclerosis and other motor neuron disorders, progressive neural muscular atrophy, retinitis pigmentosa, hereditary ataxias, multiple sclerosis and other demyelinating diseases, bacterial and viral meningitis, brain abscess, subdural empyema, epidural abscess, suppurative intracranial thrombophlebitis, myelitis and radiculitis, viral central nervous system disease, prion diseases including kuru, Creutzfeldt-Jakob disease, and Gerstmann-

25 Straussler-Scheinker syndrome, fatal familial insomnia, nutritional and metabolic diseases of the nervous system, neurofibromatosis, tuberous sclerosis, cerebelloretinal hemangioblastomatosis, encephalotrigeminal syndrome, mental retardation and other developmental disorders of the central nervous system, cerebral palsy, neuroskeletal disorders, autonomic nervous system disorders, cranial nerve disorders, spinal cord diseases, muscular dystrophy and other neuromuscular disorders,

30 peripheral nervous system disorders, dermatomyositis and polymyositis, inherited, metabolic, endocrine, and toxic myopathies, myasthenia gravis, periodic paralysis, mental disorders including mood, anxiety, and schizophrenic disorders, akathisia, amnesia, catatonia, diabetic neuropathy, tardive dyskinesia, dystonias, paranoid psychoses, postherpetic neuralgia, and Tourette's disorder; and a cell proliferative disorder such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis,

35 cirrhosis, hepatitis, mixed connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnal

hemoglobinuria, polycythemia vera, psoriasis, primary thrombocythemia, and cancers including adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus. The polynucleotide sequences encoding NuABP may be used in Southern or northern analysis, dot blot, or other membrane-based technologies; in PCR technologies; in dipstick, pin, and multiformat ELISA-like assays; and in microarrays utilizing fluids or tissues from patients to detect altered NuABP expression. Such qualitative or quantitative methods are well known in the art.

In a particular aspect, the nucleotide sequences encoding NuABP may be useful in assays that detect the presence of associated disorders, particularly those mentioned above. The nucleotide sequences encoding NuABP may be labeled by standard methods and added to a fluid or tissue sample from a patient under conditions suitable for the formation of hybridization complexes. After a suitable incubation period, the sample is washed and the signal is quantified and compared with a standard value. If the amount of signal in the patient sample is significantly altered in comparison to a control sample then the presence of altered levels of nucleotide sequences encoding NuABP in the sample indicates the presence of the associated disorder. Such assays may also be used to evaluate the efficacy of a particular therapeutic treatment regimen in animal studies, in clinical trials, or to monitor the treatment of an individual patient.

In order to provide a basis for the diagnosis of a disorder associated with expression of NuABP, a normal or standard profile for expression is established. This may be accomplished by combining body fluids or cell extracts taken from normal subjects, either animal or human, with a sequence, or a fragment thereof, encoding NuABP, under conditions suitable for hybridization or amplification. Standard hybridization may be quantified by comparing the values obtained from normal subjects with values from an experiment in which a known amount of a substantially purified polynucleotide is used. Standard values obtained in this manner may be compared with values obtained from samples from patients who are symptomatic for a disorder. Deviation from standard values is used to establish the presence of a disorder.

Once the presence of a disorder is established and a treatment protocol is initiated, hybridization assays may be repeated on a regular basis to determine if the level of expression in the patient begins to approximate that which is observed in the normal subject. The results obtained from successive assays may be used to show the efficacy of treatment over a period ranging from several days to months.

With respect to cancer, the presence of an abnormal amount of transcript (either under- or overexpressed) in biopsied tissue from an individual may indicate a predisposition for the

development of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

5 Additional diagnostic uses for oligonucleotides designed from the sequences encoding NuABP may involve the use of PCR. These oligomers may be chemically synthesized, generated enzymatically, or produced in vitro. Oligomers will preferably contain a fragment of a polynucleotide encoding NuABP, or a fragment of a polynucleotide complementary to the polynucleotide encoding NuABP, and will be employed under optimized conditions for identification of a specific gene or
10 condition. Oligomers may also be employed under less stringent conditions for detection or quantification of closely related DNA or RNA sequences.

Methods which may also be used to quantify the expression of NuABP include radiolabeling or biotinylating nucleotides, coamplification of a control nucleic acid, and interpolating results from standard curves. (See, e.g., Melby, P.C. et al. (1993) J. Immunol. Methods 159:235-244; Duplaa, C.
15 et al. (1993) Anal. Biochem. 212:229-236.) The speed of quantitation of multiple samples may be accelerated by running the assay in a high-throughput format where the oligomer of interest is presented in various dilutions and a spectrophotometric or colorimetric response gives rapid quantitation.

In further embodiments, oligonucleotides or longer fragments derived from any of the
20 polynucleotide sequences described herein may be used as targets in a microarray. The microarray can be used to monitor the expression level of large numbers of genes simultaneously and to identify genetic variants, mutations, and polymorphisms. This information may be used to determine gene function, to understand the genetic basis of a disorder, to diagnose a disorder, and to develop and monitor the activities of therapeutic agents.

25 Microarrays may be prepared, used, and analyzed using methods known in the art. (See, e.g., Brennan, T.M. et al. (1995) U.S. Patent No. 5,474,796; Schena, M. et al. (1996) Proc. Natl. Acad. Sci. USA 93:10614-10619; Baldeschweiler et al. (1995) PCT application WO95/251116; Shalon, D. et al. (1995) PCT application WO95/35505; Heller, R.A. et al. (1997) Proc. Natl. Acad. Sci. USA 94:2150-2155; and Heller, M.J. et al. (1997) U.S. Patent No. 5,605,662.)

30 In another embodiment of the invention, nucleic acid sequences encoding NuABP may be used to generate hybridization probes useful in mapping the naturally occurring genomic sequence. The sequences may be mapped to a particular chromosome, to a specific region of a chromosome, or to artificial chromosome constructions, e.g., human artificial chromosomes (HACs), yeast artificial chromosomes (YACs), bacterial artificial chromosomes (BACs), bacterial P1 constructions, or single
35 chromosome cDNA libraries. (See, e.g., Harrington, J.J. et al. (1997) Nat. Genet. 15:345-355; Price,

C.M. (1993) Blood Rev. 7:127-134; and Trask, B.J. (1991) Trends Genet. 7:149-154.)

Fluorescent in situ hybridization (FISH) may be correlated with other physical chromosome mapping techniques and genetic map data. (See, e.g., Heinz-Ulrich, et al. (1995) in Meyers, supra, pp. 965-968.) Examples of genetic map data can be found in various scientific journals or at the

5 Online Mendelian Inheritance in Man (OMIM) World Wide Web site. Correlation between the location of the gene encoding NuABP on a physical chromosomal map and a specific disorder, or a predisposition to a specific disorder, may help define the region of DNA associated with that disorder. The nucleotide sequences of the invention may be used to detect differences in gene sequences among normal, carrier, and affected individuals.

10 In situ hybridization of chromosomal preparations and physical mapping techniques, such as linkage analysis using established chromosomal markers, may be used for extending genetic maps. Often the placement of a gene on the chromosome of another mammalian species, such as mouse, may reveal associated markers even if the number or arm of a particular human chromosome is not known. New sequences can be assigned to chromosomal arms by physical mapping. This provides
15 valuable information to investigators searching for disease genes using positional cloning or other gene discovery techniques. Once the disease or syndrome has been crudely localized by genetic linkage to a particular genomic region, e.g., ataxia-telangiectasia to 11q22-23, any sequences mapping to that area may represent associated or regulatory genes for further investigation. (See, e.g., Gatti, R.A. et al. (1988) Nature 336:577-580.) The nucleotide sequence of the subject invention may also be
20 used to detect differences in the chromosomal location due to translocation, inversion, etc., among normal, carrier, or affected individuals.

In another embodiment of the invention, NuABP, its catalytic or immunogenic fragments, or oligopeptides thereof can be used for screening libraries of compounds in any of a variety of drug screening techniques. The fragment employed in such screening may be free in solution, affixed to a
25 solid support, borne on a cell surface, or located intracellularly. The formation of binding complexes between NuABP and the agent being tested may be measured.

Another technique for drug screening provides for high throughput screening of compounds having suitable binding affinity to the protein of interest. (See, e.g., Geysen, et al. (1984) PCT application WO84/03564.) In this method, large numbers of different small test compounds are
30 synthesized on a solid substrate. The test compounds are reacted with NuABP, or fragments thereof, and washed. Bound NuABP is then detected by methods well known in the art. Purified NuABP can also be coated directly onto plates for use in the aforementioned drug screening techniques. Alternatively, non-neutralizing antibodies can be used to capture the peptide and immobilize it on a solid support.

35 In another embodiment, one may use competitive drug screening assays in which neutralizing

antibodies capable of binding NuABP specifically compete with a test compound for binding NuABP. In this manner, antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with NuABP.

In additional embodiments, the nucleotide sequences which encode NuABP may be used in any molecular biology techniques that have yet to be developed, provided the new techniques rely on properties of nucleotide sequences that are currently known, including, but not limited to, such properties as the triplet genetic code and specific base pair interactions.

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. The following embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever.

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. The following preferred specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever.

The disclosures of all patents, applications, and publications mentioned above and below, in particular U.S. Ser. No. 60/117,905 and U.S. Ser. No. 60/117,904, are hereby expressly incorporated by reference.

20

EXAMPLES

I. Construction of cDNA Libraries

RNA was purchased from Clontech or isolated from tissues described in Table 4. Some tissues were homogenized and lysed in guanidinium isothiocyanate, while others were homogenized and lysed in phenol or in a suitable mixture of denaturants, such as TRIZOL (Life Technologies), a monophasic solution of phenol and guanidine isothiocyanate. The resulting lysates were centrifuged over CsCl cushions or extracted with chloroform. RNA was precipitated from the lysates with either isopropanol or sodium acetate and ethanol, or by other routine methods.

Phenol extraction and precipitation of RNA were repeated as necessary to increase RNA purity. In some cases, RNA was treated with DNase. For most libraries, poly(A+) RNA was isolated using oligo d(T)-coupled paramagnetic particles (Promega), OLIGOTEX latex particles (QIAGEN, Chatsworth CA), or an OLIGOTEX mRNA purification kit (QIAGEN). Alternatively, RNA was isolated directly from tissue lysates using other RNA isolation kits, e.g., the POLY(A)PURE mRNA purification kit (Ambion, Austin TX).

In some cases, Stratagene was provided with RNA and constructed the corresponding cDNA libraries. Otherwise, cDNA was synthesized and cDNA libraries were constructed with the UNIZAP

vector system (Stratagene) or SUPERScript plasmid system (Life Technologies), using the recommended procedures or similar methods known in the art. (See, e.g., Ausubel, 1997, *supra*, units 5.1-6.6.) Reverse transcription was initiated using oligo d(T) or random primers. Synthetic oligonucleotide adapters were ligated to double stranded cDNA, and the cDNA was digested with the appropriate restriction enzyme or enzymes. For most libraries, the cDNA was size-selected (300-1000 bp) using SEPHACRYL S1000, SEPHAROSE CL2B, or SEPHAROSE CL4B column chromatography (Amersham Pharmacia Biotech) or preparative agarose gel electrophoresis. cDNAs were ligated into compatible restriction enzyme sites of the polylinker of a suitable plasmid, e.g., PBLUEScript plasmid (Stratagene), PSPOrt1 plasmid (Life Technologies), or pINCY (Incyte Pharmaceuticals, Palo Alto CA). Recombinant plasmids were transformed into competent *E. coli* cells including XL1-Blue, XL1-BlueMRF, or SOLR from Stratagene or DH5 α , DH10B, or ElectroMAX DH10B from Life Technologies.

II. Isolation of cDNA Clones

Plasmids were recovered from host cells by *in vivo* excision using the UNIZAP vector system (Stratagene) or by cell lysis. Plasmids were purified using at least one of the following: a Magic or WIZARD Minipreps DNA purification system (Promega); an AGTC Miniprep purification kit (Edge Biosystems, Gaithersburg MD); and QIAWELL 8 Plasmid, QIAWELL 8 Plus Plasmid, QIAWELL 8 Ultra Plasmid purification systems or the R.E.A.L. PREP 96 plasmid purification kit from QIAGEN. Following precipitation, plasmids were resuspended in 0.1 ml of distilled water and stored, with or without lyophilization, at 4°C.

Alternatively, plasmid DNA was amplified from host cell lysates using direct link PCR in a high-throughput format (Rao, V.B. (1994) Anal. Biochem. 216:1-14). Host cell lysis and thermal cycling steps were carried out in a single reaction mixture. Samples were processed and stored in 384-well plates, and the concentration of amplified plasmid DNA was quantified fluorometrically using PICOGREEN dye (Molecular Probes, Eugene OR) and a FLUOROSKAN II fluorescence scanner (Labsystems Oy, Helsinki, Finland).

III. Sequencing and Analysis

cDNA sequencing reactions were processed using standard methods or high-throughput instrumentation such as the ABI CATALYST 800 (Perkin-Elmer) thermal cycler or the PTC-200 thermal cycler (MJ Research) in conjunction with the HYDRA microdispenser (Robbins Scientific) or the MICROLAB 2200 (Hamilton) liquid transfer system. cDNA sequencing reactions were prepared using reagents provided by Amersham Pharmacia Biotech or supplied in ABI sequencing kits such as the ABI PRISM BIGDYE Terminator cycle sequencing ready reaction kit (Perkin-Elmer). Electrophoretic separation of cDNA sequencing reactions and detection of labeled polynucleotides were carried out using the MEGABACE 1000 DNA sequencing system (Molecular Dynamics); the

ABI PRISM 373 or 377 sequencing system (Perkin-Elmer) in conjunction with standard ABI protocols and base calling software; or other sequence analysis systems known in the art. Reading frames within the cDNA sequences were identified using standard methods (reviewed in Ausubel, 1997, *supra*, unit 7.7). Some of the cDNA sequences were selected for extension using the techniques disclosed in Example V.

The polynucleotide sequences derived from cDNA sequencing were assembled and analyzed using a combination of software programs which utilize algorithms well known to those skilled in the art. Table 5 summarizes the tools, programs, and algorithms used and provides applicable descriptions, references, and threshold parameters. The first column of Table 5 shows the tools, programs, and algorithms used, the second column provides brief descriptions thereof, the third column presents appropriate references, all of which are incorporated by reference herein in their entirety, and the fourth column presents, where applicable, the scores, probability values, and other parameters used to evaluate the strength of a match between two sequences (the higher the score, the greater the homology between two sequences). Sequences were analyzed using MACDNASIS PRO software (Hitachi Software Engineering, South San Francisco CA) and LASERGENE software (DNASTAR). Polynucleotide and polypeptide sequence alignments were generated using the default parameters specified by the clustal algorithm as incorporated into the MEGALIGN multisequence alignment program (DNASTAR), which also calculates the percent identity between aligned sequences.

The polynucleotide sequences were validated by removing vector, linker, and polyA sequences and by masking ambiguous bases, using algorithms and programs based on BLAST, dynamic programming, and dinucleotide nearest neighbor analysis. The sequences were then queried against a selection of public databases such as the GenBank primate, rodent, mammalian, vertebrate, and eukaryote databases, and BLOCKS, PRINTS, DOMO, PRODOM, and PFAM to acquire annotation using programs based on BLAST, FASTA, and BLIMPS. The sequences were assembled into full length polynucleotide sequences using programs based on Phred, Phrap, and Consed, and were screened for open reading frames using programs based on GeneMark, BLAST, and FASTA. The full length polynucleotide sequences were translated to derive the corresponding full length amino acid sequences, and these full length sequences were subsequently analyzed by querying against databases such as the GenBank databases (described above), SwissProt, BLOCKS, PRINTS, DOMO, PRODOM, Prosite, and Hidden Markov Model (HMM)-based protein family databases such as PFAM. HMM is a probabilistic approach which analyzes consensus primary structures of gene families. (See, e.g., Eddy, S.R. (1996) *Curr. Opin. Struct. Biol.* 6:361-365.)

The programs described above for the assembly and analysis of full length polynucleotide and amino acid sequences were also used to identify polynucleotide sequence fragments from SEQ ID

NO:56-110. Fragments from about 20 to about 4000 nucleotides which are useful in hybridization and amplification technologies were described in The Invention section above.

IV. Northern Analysis

Northern analysis is a laboratory technique used to detect the presence of a transcript of a gene and involves the hybridization of a labeled nucleotide sequence to a membrane on which RNAs from a particular cell type or tissue have been bound. (See, e.g., Sambrook, supra, ch. 7; Ausubel, 1995, supra, ch. 4 and 16.)

Analogous computer techniques applying BLAST were used to search for identical or related molecules in nucleotide databases such as GenBank or LIFESEQ (Incyte Pharmaceuticals). This analysis is much faster than multiple membrane-based hybridizations. In addition, the sensitivity of the computer search can be modified to determine whether any particular match is categorized as exact or similar. The basis of the search is the product score, which is defined as:

$$\frac{\% \text{ sequence identity} \times \% \text{ maximum BLAST score}}{100}$$

The product score takes into account both the degree of similarity between two sequences and the length of the sequence match. For example, with a product score of 40, the match will be exact within a 1% to 2% error, and, with a product score of 70, the match will be exact. Similar molecules are usually identified by selecting those which show product scores between 15 and 40, although lower scores may identify related molecules.

The results of northern analyses are reported as a percentage distribution of libraries in which the transcript encoding NuABP occurred. Analysis involved the categorization of cDNA libraries by organ/tissue and disease. The organ/tissue categories included cardiovascular, dermatologic, developmental, endocrine, gastrointestinal, hematopoietic/immune, musculoskeletal, nervous, reproductive, and urologic. The disease/condition categories included cancer, inflammation, trauma, cell proliferation, neurological, and pooled. For each category, the number of libraries expressing the sequence of interest was counted and divided by the total number of libraries across all categories. Percentage values of tissue-specific and disease- or condition-specific expression are reported in Table 3.

V. Extension of NuABP Encoding Polynucleotides

The full length nucleic acid sequences of SEQ ID NO:56-110 were produced by extension of an appropriate fragment of the full length molecule using oligonucleotide primers designed from this fragment. One primer was synthesized to initiate 5' extension of the known fragment, and the other primer, to initiate 3' extension of the known fragment. The initial primers were designed using OLIGO 4.06 software (National Biosciences), or another appropriate program, to be about 22 to 30 nucleotides in length, to have a GC content of about 50% or more, and to anneal to the target

sequence at temperatures of about 68°C to about 72°C. Any stretch of nucleotides which would result in hairpin structures and primer-primer dimerizations was avoided.

Selected human cDNA libraries were used to extend the sequence. If more than one extension was necessary or desired, additional or nested sets of primers were designed.

5 High fidelity amplification was obtained by PCR using methods well known in the art. PCR was performed in 96-well plates using the PTC-200 thermal cycler (MJ Research, Inc.). The reaction mix contained DNA template, 200 nmol of each primer, reaction buffer containing Mg^{2+} , $(NH_4)_2SO_4$, and β -mercaptoethanol, Taq DNA polymerase (Amersham Pharmacia Biotech), ELONGASE enzyme (Life Technologies), and Pfu DNA polymerase (Stratagene), with the following parameters for primer pair PCI A and PCI B: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 60°C, 1 min; Step 4: 68°C, 2 min; Step 5: Steps 2, 3, and 4 repeated 20 times; Step 6: 68°C, 5 min; Step 7: storage at 4°C. In the
10 alternative, the parameters for primer pair T7 and SK+ were as follows: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 57°C, 1 min; Step 4: 68°C, 2 min; Step 5: Steps 2, 3, and 4 repeated 20 times; Step 6: 68°C, 5 min; Step 7: storage at 4°C.

15 The concentration of DNA in each well was determined by dispensing 100 μ l PICOGREEN quantitation reagent (0.25% (v/v) PICOGREEN; Molecular Probes, Eugene OR) dissolved in 1X TE and 0.5 μ l of undiluted PCR product into each well of an opaque fluorimeter plate (Corning Costar, Acton MA), allowing the DNA to bind to the reagent. The plate was scanned in a Fluoroskan II (Labsystems Oy, Helsinki, Finland) to measure the fluorescence of the sample and to quantify the
20 concentration of DNA. A 5 μ l to 10 μ l aliquot of the reaction mixture was analyzed by electrophoresis on a 1 % agarose mini-gel to determine which reactions were successful in extending the sequence.

The extended nucleotides were desalted and concentrated, transferred to 384-well plates, digested with CviII cholera virus endonuclease (Molecular Biology Research, Madison WI), and
25 sonicated or sheared prior to religation into pUC 18 vector (Amersham Pharmacia Biotech). For shotgun sequencing, the digested nucleotides were separated on low concentration (0.6 to 0.8%) agarose gels, fragments were excised, and agar digested with Agar ACE (Promega). Extended clones were religated using T4 ligase (New England Biolabs, Beverly MA) into pUC 18 vector (Amersham Pharmacia Biotech), treated with Pfu DNA polymerase (Stratagene) to fill-in restriction site
30 overhangs, and transfected into competent *E. coli* cells. Transformed cells were selected on antibiotic-containing media, individual colonies were picked and cultured overnight at 37°C in 384-well plates in LB/2x carb liquid media.

The cells were lysed, and DNA was amplified by PCR using Taq DNA polymerase (Amersham Pharmacia Biotech) and Pfu DNA polymerase (Stratagene) with the following
35 parameters: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 60°C, 1 min; Step 4: 72°C, 2 min;

Step 5: steps 2, 3, and 4 repeated 29 times; Step 6: 72°C, 5 min; Step 7: storage at 4°C. DNA was quantified by PICOGREEN reagent (Molecular Probes) as described above. Samples with low DNA recoveries were reamplified using the same conditions as described above. Samples were diluted with 20% dimethylsulfoxide (1:2, v/v), and sequenced using DYENAMIC energy transfer sequencing
5 primers and the DYENAMIC DIRECT kit (Amersham Pharmacia Biotech) or the ABI PRISM BIGDYE Terminator cycle sequencing ready reaction kit (Perkin-Elmer).

In like manner, the nucleotide sequences of SEQ ID NO:56-110 are used to obtain 5' regulatory sequences using the procedure above, oligonucleotides designed for such extension, and an appropriate genomic library.

10 VI. Labeling and Use of Individual Hybridization Probes

Hybridization probes derived from SEQ ID NO:56-110 are employed to screen cDNAs, genomic DNAs, or mRNAs. Although the labeling of oligonucleotides, consisting of about 20 base pairs, is specifically described, essentially the same procedure is used with larger nucleotide fragments. Oligonucleotides are designed using state-of-the-art software such as OLIGO 4.06
15 software (National Biosciences) and labeled by combining 50 pmol of each oligomer, 250 µCi of [γ -³²P] adenosine triphosphate (Amersham Pharmacia Biotech), and T4 polynucleotide kinase (DuPont NEN, Boston MA). The labeled oligonucleotides are substantially purified using a SEPHADEX G-25 superfine size exclusion dextran bead column (Amersham Pharmacia Biotech). An aliquot containing 10⁷ counts per minute of the labeled probe is used in a typical membrane-based
20 hybridization analysis of human genomic DNA digested with one of the following endonucleases: Ase I, Bgl II, Eco RI, Pst I, Xba I, or Pvu II (DuPont NEN).

The DNA from each digest is fractionated on a 0.7% agarose gel and transferred to nylon membranes (Nytran Plus, Schleicher & Schuell, Durham NH). Hybridization is carried out for 16 hours at 40°C. To remove nonspecific signals, blots are sequentially washed at room temperature
25 under conditions of up to, for example, 0.1 x saline sodium citrate and 0.5% sodium dodecyl sulfate. Hybridization patterns are visualized using autoradiography or an alternative imaging means and compared.

VII. Microarrays

A chemical coupling procedure and an ink jet device can be used to synthesize array
30 elements on the surface of a substrate. (See, e.g., Baldeschweiler, *supra*.) An array analogous to a dot or slot blot may also be used to arrange and link elements to the surface of a substrate using thermal, UV, chemical, or mechanical bonding procedures. A typical array may be produced by hand or using available methods and machines and contain any appropriate number of elements. After hybridization, nonhybridized probes are removed and a scanner used to determine the levels and
35 patterns of fluorescence. The degree of complementarity and the relative abundance of each probe

which hybridizes to an element on the microarray may be assessed through analysis of the scanned images.

Full-length cDNAs, Expressed Sequence Tags (ESTs), or fragments thereof may comprise the elements of the microarray. Fragments suitable for hybridization can be selected using software well known in the art such as LASERGENE software (DNASTAR). Full-length cDNAs, ESTs, or fragments thereof corresponding to one of the nucleotide sequences of the present invention, or selected at random from a cDNA library relevant to the present invention, are arranged on an appropriate substrate, e.g., a glass slide. The cDNA is fixed to the slide using, e.g., UV cross-linking followed by thermal and chemical treatments and subsequent drying. (See, e.g., Schena, M. et al. (1995) Science 270:467-470; Shalon, D. et al. (1996) Genome Res. 6:639-645.) Fluorescent probes are prepared and used for hybridization to the elements on the substrate. The substrate is analyzed by procedures described above.

VIII. Complementary Polynucleotides

Sequences complementary to the NuABP-encoding sequences, or any parts thereof, are used to detect, decrease, or inhibit expression of naturally occurring NuABP. Although use of oligonucleotides comprising from about 15 to 30 base pairs is described, essentially the same procedure is used with smaller or with larger sequence fragments. Appropriate oligonucleotides are designed using OLIGO 4.06 software (National Biosciences) and the coding sequence of NuABP. To inhibit transcription, a complementary oligonucleotide is designed from the most unique 5' sequence and used to prevent promoter binding to the coding sequence. To inhibit translation, a complementary oligonucleotide is designed to prevent ribosomal binding to the NuABP-encoding transcript.

IX. Expression of NuABP

Expression and purification of NuABP is achieved using bacterial or virus-based expression systems. For expression of NuABP in bacteria, cDNA is subcloned into an appropriate vector containing an antibiotic resistance gene and an inducible promoter that directs high levels of cDNA transcription. Examples of such promoters include, but are not limited to, the *trp-lac* (*tac*) hybrid promoter and the T5 or T7 bacteriophage promoter in conjunction with the *lac* operator regulatory element. Recombinant vectors are transformed into suitable bacterial hosts, e.g., BL21(DE3). Antibiotic resistant bacteria express NuABP upon induction with isopropyl beta-D-thiogalactopyranoside (IPTG). Expression of NuABP in eukaryotic cells is achieved by infecting insect or mammalian cell lines with recombinant Autographica californica nuclear polyhedrosis virus (AcMNPV), commonly known as baculovirus. The nonessential polyhedrin gene of baculovirus is replaced with cDNA encoding NuABP by either homologous recombination or bacterial-mediated transposition involving transfer plasmid intermediates. Viral infectivity is maintained and the strong polyhedrin promoter drives high levels of cDNA transcription. Recombinant baculovirus is used to

infect Spodoptera frugiperda (Sf9) insect cells in most cases, or human hepatocytes, in some cases. Infection of the latter requires additional genetic modifications to baculovirus. (See Engelhard, E.K. et al. (1994) Proc. Natl. Acad. Sci. USA 91:3224-3227; Sandig, V. et al. (1996) Hum. Gene Ther. 7:1937-1945.)

5 In most expression systems, NuABP is synthesized as a fusion protein with, e.g., glutathione S-transferase (GST) or a peptide epitope tag, such as FLAG or 6-His, permitting rapid, single-step, affinity-based purification of recombinant fusion protein from crude cell lysates. GST, a 26-kilodalton enzyme from Schistosoma japonicum, enables the purification of fusion proteins on immobilized glutathione under conditions that maintain protein activity and antigenicity (Amersham
10 Pharmacia Biotech). Following purification, the GST moiety can be proteolytically cleaved from NuABP at specifically engineered sites. FLAG, an 8-amino acid peptide, enables immunoaffinity purification using commercially available monoclonal and polyclonal anti-FLAG antibodies (Eastman Kodak). 6-His, a stretch of six consecutive histidine residues, enables purification on metal-chelate
15 supra, ch. 10 and 16). Purified NuABP obtained by these methods can be used directly in the following activity assay.

X. Demonstration of NuABP Activity

NuABP activity is measured by its ability to stimulate transcription of a reporter gene (Liu, H.Y. et al. (1997) EMBO J. 16(17):5289-5298.) The assay entails the use of a well characterized
20 reporter gene construct, LexA_{op}-LacZ, that consists of LexA DNA transcriptional control elements (LexA_{op}) fused to sequences encoding the E. coli LacZ enzyme. The methods for constructing and expressing fusions genes, introducing them into cells, and measuring LacZ enzyme activity, are well known to those skilled in the art. Sequences encoding NuABP are cloned into a plasmid that directs the synthesis of a fusion protein, LexA-NuABP, consisting of NuABP and a DNA binding domain
25 derived from the LexA transcription factor. The resulting plasmid, encoding a LexA-NuABP fusion protein, is introduced into yeast cells along with a plasmid containing the LexA_{op}-LacZ reporter gene. The amount of LacZ enzyme activity associated with LexA-NuABP transfected cells, relative to control cells, is proportional to the amount of transcription stimulated by the NuABP.

XI. Functional Assays

30 NuABP function is assessed by expressing the sequences encoding NuABP at physiologically elevated levels in mammalian cell culture systems. cDNA is subcloned into a mammalian expression vector containing a strong promoter that drives high levels of cDNA expression. Vectors of choice include pCMV SPORT (Life Technologies) and pCR3.1 (Invitrogen, Carlsbad CA), both of which contain the cytomegalovirus promoter. 5-10 µg of recombinant vector
35 are transiently transfected into a human cell line, for example, an endothelial or hematopoietic cell

line. using either liposome formulations or electroporation. 1-2 μ g of an additional plasmid containing sequences encoding a marker protein are co-transfected. Expression of a marker protein provides a means to distinguish transfected cells from nontransfected cells and is a reliable predictor of cDNA expression from the recombinant vector. Marker proteins of choice include, e.g., Green
5 Fluorescent Protein (GFP; Clontech), CD64, or a CD64-GFP fusion protein. Flow cytometry (FCM), an automated, laser optics-based technique, is used to identify transfected cells expressing GFP or CD64-GFP and to evaluate the apoptotic state of the cells and other cellular properties. FCM detects and quantifies the uptake of fluorescent molecules that diagnose events preceding or coincident with
10 cell death. These events include changes in nuclear DNA content as measured by staining of DNA with propidium iodide; changes in cell size and granularity as measured by forward light scatter and 90 degree side light scatter; down-regulation of DNA synthesis as measured by decrease in bromodeoxyuridine uptake; alterations in expression of cell surface and intracellular proteins as measured by reactivity with specific antibodies; and alterations in plasma membrane composition as measured by the binding of fluorescein-conjugated Annexin V protein to the cell surface. Methods in
15 flow cytometry are discussed in Ormerod, M.G. (1994) Flow Cytometry, Oxford, New York NY.

The influence of NuABP on gene expression can be assessed using highly purified populations of cells transfected with sequences encoding NuABP and either CD64 or CD64-GFP. CD64 and CD64-GFP are expressed on the surface of transfected cells and bind to conserved regions of human immunoglobulin G (IgG). Transfected cells are efficiently separated from nontransfected
20 cells using magnetic beads coated with either human IgG or antibody against CD64 (DYNAL, Lake Success NY). mRNA can be purified from the cells using methods well known by those of skill in the art. Expression of mRNA encoding NuABP and other genes of interest can be analyzed by northern analysis or microarray techniques.

XII. Production of NuABP Specific Antibodies

25 NuABP substantially purified using polyacrylamide gel electrophoresis (PAGE; see, e.g., Harrington, M.G. (1990) *Methods Enzymol.* 182:488-495), or other purification techniques, is used to immunize rabbits and to produce antibodies using standard protocols.

Alternatively, the NuABP amino acid sequence is analyzed using LASERGENE software (DNASTAR) to determine regions of high immunogenicity, and a corresponding oligopeptide is
30 synthesized and used to raise antibodies by means known to those of skill in the art. Methods for selection of appropriate epitopes, such as those near the C-terminus or in hydrophilic regions are well described in the art. (See, e.g., Ausubel, 1995, supra, ch. 11.)

Typically, oligopeptides of about 15 residues in length are synthesized using an ABI 431A peptide synthesizer (Perkin-Elmer) using fmoc-chemistry and coupled to KLH (Sigma-Aldrich, St.
35 Louis MO) by reaction with N-maleimidobenzoyl-N-hydroxysuccinimide ester (MBS) to increase

immunogenicity. (See, e.g., Ausubel, 1995, supra.) Rabbits are immunized with the oligopeptide-KLH complex in complete Freund's adjuvant. Resulting antisera are tested for antipeptide and anti-NuABP activity by, for example, binding the peptide or NuABP to a substrate, blocking with 1% BSA, reacting with rabbit antisera, washing, and reacting with radio-iodinated goat anti-rabbit IgG.

5 **XIII. Purification of Naturally Occurring NuABP Using Specific Antibodies**

Naturally occurring or recombinant NuABP is substantially purified by immunoaffinity chromatography using antibodies specific for NuABP. An immunoaffinity column is constructed by covalently coupling anti-NuABP antibody to an activated chromatographic resin, such as CNBr-activated SEPHAROSE (Amersham Pharmacia Biotech). After the coupling, the resin is
10 blocked and washed according to the manufacturer's instructions.

Media containing NuABP are passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of NuABP (e.g., high ionic strength buffers in the presence of detergent). The column is eluted under conditions that disrupt antibody/NuABP binding (e.g., a buffer of pH 2 to pH 3, or a high concentration of a chaotrope, such
15 as urea or thiocyanate ion), and NuABP is collected.

XIV. Identification of Molecules Which Interact with NuABP

NuABP, or biologically active fragments thereof, are labeled with ¹²⁵I Bolton-Hunter reagent. (See, e.g., Bolton A.E. and W.M. Hunter (1973) Biochem. J. 133:529-539.) Candidate molecules previously arrayed in the wells of a multi-well plate are incubated with the labeled NuABP, washed,
20 and any wells with labeled NuABP complex are assayed. Data obtained using different concentrations of NuABP are used to calculate values for the number, affinity, and association of NuABP with the candidate molecules.

Various modifications and variations of the described methods and systems of the invention will be apparent to those skilled in the art without departing from the scope and spirit of the invention.
25 Although the invention has been described in connection with certain embodiments, it should be understood that the invention as claimed should not be unduly limited to such specific embodiments. Indeed, various modifications of the described modes for carrying out the invention which are obvious to those skilled in molecular biology or related fields are intended to be within the scope of the following claims.

TABLE 1

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
1	56	025733	SPLNFET01	025733H1 and 025733X307D2 (SPLNFET01), 1519809F1 and 1519809T1 (BLADTUT04), 1526288T6 (UCMCL5T01), 1595557X16C1 and 1595557X19C1 (BRAINT014), 19033359F6 (OVARNOT07), 2417225F6 (HNT3AZT01), 4283542H1 (LIVRDIR01)
2	57	079702	SYNORAB01	002190H1 (U937NOT01), 079479F1 and 079702H1 (SYNORAB01), 125223T6 (LUNGNOT01), 371006R6 (LUNGNOT02), 2129460T6 (KIDNNOT05), 2999366H1 (TLYMNOT06), 3031905F6 (TLYMNOT05), 4949863H1 (SINTNOT25)
3	58	116208	KIDNNOT01	116208H1 and 116208R1 (KIDNNOT01), 2293058R6 (BRAINON01), 3731418H1 and 3731418T6 (SMCCNON03)
4	59	179261	PLACNOB01	179261H1 (PLACNOB01), 3666231F6 and 3666231T6 (PANCNOT16)
5	60	259161	HNT2RAT01	259161H1 (HNT2RAT01), 1005021R6 (BRSTNOT03), 2634660H1 (COLNTUT15), 2894335H1 (KIDNTUT14), 2924845H1 (SININOT04), 3659440H1 (ENDPNOT02), SBMA02955F1, SBMA03577F1, SBMA01445F1, SBMA00985F1, SBMA01499F1
6	61	320087	EOSIHET02	016657F1 (HUVELPB01), 320087H1 (EOSIHET02), 824110R1 (PROSNOT06), 987467H1 (LVENNOT03), 1235752F1 (LUNGFET03), 1361280F1 (LUNGNOT12), 1389740H1 (EOSINOT01), 1534332F1 (SPLNNOT04), 1813754F6 (SKINBIT01), 4184915H1 (BRSTNOT31), 5306522H1 (MONOTXT02)
7	62	491271	HNT2AGT01	363816X3 and 363816X9 (PROSNOT01), 491271F1, 491271H1 and 491271T6 (HNT2AGT01), 967354R6, 967354X15 and 967354X27 (BRSTNOT05), 2733444H1 (OVARNTUT04)
8	63	585172	PROSNOT02	395188R6 (TMLR2DT01), 585172H1 (PROSNOT02), 864269T1 (BRAITUT03), 1417965F1 (KIDNNOT09)
9	64	615200	COLNTUT02	615200H1 and 615200R6 (COLNTUT02), 1213980R1 (BRSTTUT01), SBPA02731D1, SBPA00184D1
10	65	997067	KIDNTUT01	125981X3 (LUNGNOT01), 997067H1, 997067R6 and 997067T6 (KIDNTUT01), 1448201H1 (PLACNOT02), 1663447H1 (BRSTNOT09), 1889314H1 (BLADTUT07), 1918706H1 (PROSNOT06), 2699956H1 (OVARNTUT10), 2702585H1 (OVARNTUT10), 2900479H1 (DRGCNOT01), 3595727T6 (FIBPNOT01), 4309131H1 (BRAUNOT01)
11	66	144326 2	THYRNOT03	1257005F1 (MENITUT03), 1443262H1 (THYRNOT03), 1618906F6 (BRAITUT12), 2474133T6 (THPINOT03), 3594075H1 (FIBPNOT01), 4914442H1 (LIVRFET05)

TABLE 1 (cont.)

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
12	67	152164 8	BLADTUT04	292172H1 (TMLR3DT01), 819925R6 (KERANOT02), 1353913H1 (LATRTUT02), 1521648H1 and 1522364F1 (BLADTUT04), 1963178H1 (BRSTNOT04), 2342505F6 (TESTTUT02), 4899970H1 (OVARIT01), 5043585H2 (PLACFER01)
13	68	168549 4	PROSNOT15	903980X13, 903980X14 and 903980X17 (COLNNOT07), 1685494H1 (PROSNOT15), 4164127T6 (BRSTNOT32)
14	69	173082 9	BRSTTUT08	116146R1 (KIDNNOT01), 836856R1 (PROSNOT07), 1730829H1, 1730829X11C1, 1730829X12C1 and 1730829X13C1 (BRSTTUT08), 1959889R6 (BRSTNOT04), 2188079H1 (PROSNOT26), 3384625H1 (ESOGNOT04)
15	70	186464 1	PROSNOT19	1844972H1 (COLNNOT08), 1864641F6 and 1864641H1 (PROSNOT19), 3090702T6 (BRSTNOT19), 3411665H1 (BRSTTUS08), 5152366H1 (HEARFET03), 5166179H1 (MUSCDMT01)
16	71	244460 4	THPINOT03	1506658F1 (BRAITUT07), 1532034F1 (SPLNNOT04), 2444604H1 (THPINOT03)
17	72	244500 8	THPINOT03	605598X12 (BRSTTUT01), 628644H1 (KIDNNOT05), 732124R1 (LUNGNOT03), 819194R1 (KERANOT02), 1259467H1 (MENITUT03), 1363205F6 (LUNGNOT12), 1901312T6 (BLADTUT06), 2445008H1 (THPINOT03), 2681125H1 (SINIUCT01)
18	73	257246 2	HIPOAZT01	396323R6 (PITUNOT02), 863622H1 (BRAITUT03), 1848956F6 and 1848956T6 (LUNGFET03), 2345947H1 (TESTTUT02), 2396384F6 (THP1AZT01), 2572462H1 (HIPOAZT01), 2650980F6 (LUNGTUT12), 2814325H1 (OVARNOT10), 5076051H1 (COLCTUT03)
19	74	257289 2	HIPOAZT01	030596X15R1 (THPINOB01), 539564X11 (LNODNOT02), 1275514F1 and 1275514T6 (TESTTUT02), 2112383H1 (BRAITUT03), 2572892H1 (HIPOAZT01), 2986518H1 (CARGDIT01)
20	75	278567 4	BRSTNOT13	261399H1 (HNT2AGT01), 1274739F1 (TESTTUT02), 2785674H1 (BRSTNOT13)
21	76	279747 9	NPOLNOT01	302614X13 (TESTNOT04), 2797479H1 (NPOLNOT01), SAIA02597F1, SAIA00739F1, SAIA02537F1
22	77	296064 0	ADRENOT09	027211R1, 027211X1 and 027211X3 (SPLNFET01), 1401538F6 (BRAITUT08), 2496984F6 (ADRETUT05), 2960640H1 (ADRENOT09), 3211036T6 (BLADNOT08)
23	78	345405 1	SPLNNOT11	279331R6 (LIVRNOT02), 2515972T6 and 2516010T6 (LIVRTUT04), 2910726F6 (KIDNTUT15), 3454051H1 (SPLNNOT11)

TABLE 1 (cont.)

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
24	79	351064 0	CONCNOT01	556354H1 (MPHGLPT02), 581085H1 (BRAVXT05), 990636R6 (COLNNOT11), 1799185F6 and 1799185T6 (COLNNOT27), 3510640H1 (CONCNOT01), 4326648H1 (TLYMUNT01), SBHA01099F1
25	80	381508 3	TONSNOT03	2026951R6 and 2026951T6 (KERANOT02), 2300211R6 (BRSTNOT05), 2505283F6 (CONUTUT01), 3187267R6 (THYMNON04), 3815083H1 and 3815083T6 (TONSNOT03)
26	81	398845 7	LUNGNOT03	609622R6 (COLNNOT01), 1710465F6 (PROSNOT16), 3988457H1 (LUNGNOT03), SAQA00089F1, SAQA03055F1, SAQB00279F1
27	82	131890	BMARNOT02	131890H1 (BMARNOT02), 131890T6 (BMARNOT02), 132849R6 (BMARNOT02), 3357071F6 (PROSTUT16)
28	83	238642	SINTNOT02	238642H1 (SINTNOT02), 1620593F6 (BRAITUT13), 1620593H1 (BRAITUT13), 1620593T6 (BRAITUT13), 2534087F6 (BRAINOT18)
29	84	669862	CRBLNOT01	347231X7 (THYMNOT02), 669862H1 (CRBLNOT01), 2244458R6 (HIPONOT02), 2244458T6 (HIPONOT02), 2622610T6 (KERANOT02), 3536262H1 (KIDNNOT25), 4204212H1 (BRAITUT29)
30	85	100366 3	BRSTNOT03	850478T1 (NGANNOT01), 1003663H1 (BRSTNOT03), 1252179F2 (LUNGNOT03), 1293336F1 (PGANNOT03), 1813002F6 (PROSTUT12), 2101974R6 (BRAITUT02)
31	86	143255 7	BEPINON01	1314545F6 (BLADTUT02), 1432557H1 (BEPINON01), 1443311R1 (THYRNOT03), 1705738F6 (DUODNOT02), 2182184F6 (SININOT01)
32	87	144177 0	THYRNOT03	035105R1 (HUVENOB01), 1441770H1 (THYRNOT03), 1500943F1 (SINTBST01), 2542840H1 (UTRSNOT11), 4533672H1 (OVARNOT12)
33	88	145668 4	COLNFET02	1456684F6 (COLNFET02), 1456684H1 (COLNFET02), 1456684T6 (COLNFET02), 1992143H1 (CORPNOT02), 2687476F6 (LUNGNOT23), 3139175F6 (SMCCNOT02), 4746319H1 (SMCRUNT01)
34	89	160291 6	BLADNOT03	3397976X305D2 (UTRSNOT16)
35	90	169281 6	COLNNOT23	999017R6 (KIDNTUT01), 1342490T1 (COLNTUT03), 1421981F1 (KIDNNOT09), 1692816H1 (COLNNOT23), 2176832F6 (ENDCNOT03), 2451404F6 (ENDANOT01)
36	91	196819 1	BRSTNOT04	1968191H1 (BRSTNOT04), 1968191T6 (BRSTNOT04), 2752967R6 (THPLAZS08), 3281163T6 (STONFET02), 3748607H1 (UTRSNOT18)
37	92	205206 1	LIVRFET02	003803X8 (HMCINOT01), 027044X1 (SPLNFET01), 027044X101 (SPLNFET01), 2052061H1 (LIVRFET02), 3931936F6 (PROSTUT09)

TABLE 1 (cont.)

Protein SEQ ID No:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
38	93	205620 7	BEPINOT01	071525F1 (PLACNOB01), 162720R1 (ADENINB01), 270498H1 (HNT2NOT01), 1477853T1 (CORPNOT02), 1931058F6 (COLNTUT03), 2056207H1 (BEPINOT01), 2056207X11R1 (BEPINOT01), 2231060F6 (PROSNOT16), 2420063X309D4 (SCORNON02), 3424630H1 (BRSTNOR01), 3873760F6 (HEARNOT06), 3873760T6 (HEARNOT06), SBQA00627D1, SCJA02192V1, SCJA02089V1
39	94	210180 3	BRAITUT02	399584R6 (PITUNOT02), 399584T6 (PITUNOT02), 1649058F6 (PROSTUT09), 1902809F6 (OVARNOT07), 2101803H1 (BRAITUT02), 2101803R6 (BRAITUT02), 3098623H1 (CERVNOT03)
40	95	211236 2	BRAITUT03	948628R1 (PANCNOT05), 1209447T1 (BRSTNOT02), 1814624F6 (PROSNOT20), 2112362H1 (BRAITUT03), 2945621H1 (BRAITUT23), 3285663H1 (HEAONOT05), 3526403H1 (ESOGTUN01), 5032729H1 (ENDIUNT01), 5099417H1 (PROSTUS20)
41	96	211734 6	BRSTTUT02	487994R6 (HNT2AGT01), 952855R1 (SCORNON01), 952855T1 (SCORNON01), 2117346H1 (BRSTTUT02), 2458342F6 (ENDANOT01), 2731585H1 (OVRTUT04), 3475780H1 (LUNGNOT27), 3538525F6 (SEMVNOT04)
42	97	211991 7	BRSTTUT02	2119917H1 (BRSTTUT02), 2791421F6 (COLNTUT16), 2794083F6 (COLNTUT16), 5006921H1 (STOMNOT08)
43	98	212345 6	BRSTNOT07	484031H1 (HNT2RAT01), 617559F1 (PGANNOT01), 617559R1 (PGANNOT01), 1575977F1 (LNODNOT03), 2123456H1 (BRSTNOT07), 2958712H1 (ADRENOT09), 3764961H1 (BRSTNOT24)
44	99	214879 2	BRAINOT09	1732781F6 (BRSTTUT08), 2050885F6 (LIVRFET02), 2148792H1 (BRAINOT09), 2590822H1 (LUNGNOT22), 2972368T6 (HEAONOT02), SBQA00396D1, SBQA03678D1, SBQA02120D1, SBQA03269D1
45	100	275194 3	THP1AZS08	1720187X16C1 (BLADNOT06), 2751943H1 (THP1AZS08), 3492378H1 (ADRETUT07)
46	101	312891 3	LUNGUT12	2551859F6 (LUNGUT06), 3128913H1 (LUNGUT12), SBMA01861F1, SBMA02298F1, SBMA01013F1, SBMA02403F1, SBMA01362F1
47	102	328294 1	HEAONOT05	154741R6 (THP1PLB02), 155904R6 (THP1PLB02), 157816R1 (THP1PLB02), 979920H1 (TONGTUT01), 1233933T6 (LUNGFEOT03), 1657077F6 (URETTUT01), 2445017F6 (THP1NOT03), 3282941H1 (HEAONOT05), 3341633H1 (SPLNNOT09), 3517140H1 (LUNGNON03)
48	103	328665 6	HEAONOT05	898123H1 (BRSTNOT05), 3286656H1 (HEAONOT05), 3641429T6 (LUNGNOT30), 3657668F6 (ENDPNOT02)

TABLE 1 (cont.)

Protein SEQ ID No:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
49	104	349080 2	EPIGNOT01	2238441H1 (PANCUTUT02), 2700133F6 (OVARTUT10), 2700133T6 (OVARTUT10), 3490226H1 (EPIGNOT01), 3490802H1 (EPIGNOT01), 4822929H1 (PROSTUT17)
50	105	350736 6	CONCNOT01	2130284H1 (KIDNNOT05), 3507366H1 (CONCNOT01), 3557087F6 (LUNGNOT31), 4241774H1 (SYNWDIT01)
51	105	357306 0	BRONNOT01	3573060F6 (BRONNOT01), 3573060H1 (BRONNOT01), 3573060T6 (BRONNOT01), 3867263H1 (BRAITUT07), 5013346H1 (BRAXNOT03)
52	107	357366 1	BRONNOT01	3028034F6 (HEARFET02), 3152642H1 (ADRENON04), 3573661F6 (BRONNOT01), 3573661H1 (BRONNOT01), 3577568F6 (BRONNOT01)
53	108	363342 2	LIVRNOT03	033412R6 (THP1NOB01), 074123F1 (THPIPEB01), 263241H1 (HNT2AGT01), 748567R1 (BRAITUT01), 1292088T1 (PGANNOT03), 1517449T1 (PANCUTUT01), 3633422H1 (LIVRNOT03)
54	109	399337 7	LUNGNON03	3003233H1 (TLYMNOT06), 3993377H1 (LUNGNON03), 3993377T6 (LUNGNON03), 4251662F6 (BRADDIR01), SBSA02001V1
55	110	471793 6	BRAIHCT02	4717936F6 (BRAIHCT02), 4717936H1 (BRAIHCT02), 4717936T6 (BRAIHCT02)

TABLE 2 (cont.)

Polypeptide Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequence(s)	Identification/ Homologous Sequence	Analytical Methods and Databases
5	562	T29 T43 S76 S142 S165 S202 T214 Y302 S305 Y349 S385 S500 T526 S527		Y235 - D312 PFAM	DNA helicase (GI 531243; SEQ ID NO:113)	BLAST, PFAM, BLOCKS, MOTIFS
6	432	S33 S58 T166 T172 S197 T230 T261 S275 S286 S290 S298 S338 T362 S376 T407 T409 T419		E329 - A355 BLOCKS	CCAAT-box-binding transcription factor	BLOCKS, MOTIFS
7	799	T24 S33 T43 S73 T88 S91 S110 S147 T219 S262 S323 Y380 S532 S586 S756 T795		H250 - H291 Y324 - H346 Y253 - H374 Y380 - H402 PFAM	C2H2-type zinc finger protein (GI 498727)	BLAST, PFAM, BLOCKS, PRINTS, MOTIFS
8	137	S3 T38 S74 S75 S118		R85 - L97 PFAM	BTB domain/C2H2-type zinc finger protein	PFAM, PRINTS, MOTIFS
9	230	T178 S187			sirtuin type 3 (GI 5225322)	BLAST, MOTIFS
10	446	T3 S28 S32 T52 T94 T96 S135 S143 T159 T165 S171 S433		H200 - H222 Y228 - H250 Y256 - H278 Y284 - H306	zinc finger protein ZFP113 (GI 5640017)	BLAST, PFAM, BLOCKS, PRINTS, MOTIFS
11	428	S72 S92 S101 S118 S120 S125 T245 T277 S289 S315 S317 Y326 S409			Skeletal muscle BOP2 (GI 5870834; SEQ ID NO:117)	BLAST, MOTIFS

TABLE 2 (cont.)

Polypeptide Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequence(s)	Identification/ Homologous Sequence	Analytical Methods and Databases
12	590	S45 Y52 T60 S83 S90 T95 T116 T145 T233 T330 S391 S410 S411 T420 T439 T490 S521			Methyl-CpG binding protein (GI 2239126)	BLAST, MOTIFS
13	479	S15 Y29 S30 S118 T173 T183 S203 S217 Y232 S235 T255 S352 S362 Y451		Y232 - H254 H283 - H305 Y311 - H333 Y339 - H361 PFAM	SRE-ZBP (GI 936603)	BLAST, PFAM, BLOCKS, PRINTS, MOTIFS
14	433	S92 S96 T250 S319 T322 T327 S335 T344		C380 - C421 PFAM	C3HC4-type zinc finger protein	PFAM, BLOCKS, MOTIFS
15	320	T6 S27 T125 T172 S229 S232 T239 S248 S259 S266 Y267 S291			Zinc finger factor (GI 3150148)	BLAST, MOTIFS
16	179	S11 T21 S46 S140			Single-stranded DNA binding protein (csdp) (GI 1562534)	BLAST, MOTIFS
17	494	T73 Y80 S104 Y116 T192 S289 S297 T329 T364 T376 S387		C13 - H41 BLOCKS	Zinc finger transcription factor (GI 2895870)	BLAST, BLOCKS, MOTIFS
18	401	S4 S82 S97 T166 S188 S249 S279 S289 S290 S294 S319 S368 S371 S372 S378 T392 S396		P5 - K81 A114 - S179 G186 - P262 PFAM	HP1-BP74 (GI 1480112)	PFAM, BLOCKS, PRINTS, MOTIFS

TABLE 2 (cont.)

Polypeptide Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequence(s)	Identification/ Homologous Sequence	Analytical Methods and Databases
19	264	S11 S25 S76 S82 S90 S92 S96 S119 T229		F154 - H176 C180 - H202 F208 - H230 Y236 - C259 PFAM	C2H2-type zinc finger protein (GI 429188)	BLAST, PFAM, BLOCKS, PRINTS, MOTIFS
20	153	T23 S40 T44 S110 S120 T124		R42 - E141 PFAM	High mobility group- like nuclear protein (GI 2822179)	BLAST, PFAM, BLOCKS, PRINTS, MOTIFS
21	243	S20 S21 S76 S100 S104 S160 T194 S196 S212 T222 Y229		Y90 - H112 H118 - H140 Y146 - H168 Y174 - H195 PFAM	C2H2-type zinc finger protein (GI 38015)	BLAST, PFAM, BLOCKS, PRINTS, MOTIFS
22	485	T29 S34 S104 S147 T162 T248 S249 S256 S347 S452 S477		S309 - H331 H337 - H359 Y365 - H387 Y393 - H415 PFAM	BTB domain/C2H2-type zinc finger protein (GI 2843171)	BLAST, PFAM, BLOCKS, PRINTS, MOTIFS
23	160	S118		C5 - F62 C80 - F137 PFAM	LIM domain protein/CRP2 (GI 487284)	BLAST, PFAM, BLOCKS, PROFILESAN, MOTIFS
24	511	S10 T36 S75 S90 S222 T245 T259 S399 S405 Y443 S500		Y171 - P223 Y267 - K294 BLOCKS	2'-5'-oligoadenylate synthetase-related protein p56 (GI 4731857)	BLOCKS, MOTIFS
25	310	S24 S39 T69 Y104 S185 T282 T296			SIR2 family transcriptional regulatory protein (GI 2648874)	BLAST, MOTIFS

TABLE 2 (cont.)

Polypeptide Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequence(s)	Identification/ Homologous Sequence	Analytical Methods and Databases
26	331	T29 S40 S74 S257 T270 S301		V112 - R134 BLOCKS	Histone protein	BLOCKS, MOTIFS
27	200	T43 S123 T129 S167 S183 S184 S44 Y25 Y98			Zinc finger protein (g1373394)	MOTIFS BLAST
28	100			Transcription anti-terminator; bgl family: E47-I100	transcription elongation factor (g4336506)	MOTIFS BLAST BLOCKS
29	528	S204 T487 S29 S34 T48 T227 S327 T367 T423 S483 Y39 Y44 Y112 Y163	N24 N52 N100 N481	C2H2 zinc fingers: Y191-H213 Y247-H269 Y275-H297 Y331-H353 Y387-H409 Y415-H437 Y443-H465 Y471-H493	Zinc finger protein (g498721)	MOTIFS BLAST BLOCKS PFAM
30	350	T264 S305	N33 N79	C3HC4 RING finger: C230-C271	C3HC4/RING zinc finger protein (g1321818)	MOTIFS BLAST BLOCKS PFAM PROFILES CAN
31	315	S51 T94 S121 S123 S142 S143 T184 S232 S252 T36 T46 S159 S163 S168 S36 S56 T93 S104			Similar to CCAAT/enhancer-binding protein (g1947129)	MOTIFS BLAST
32	120		N98 N103	bZIP transcription factor: P21-P85		MOTIFS PFAM BLOCKS

TABLE 2 (cont.)

Polypeptide Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequence(s)	Identification/ Homologous Sequence	Analytical Methods and Databases
33	326	S59 S38 T207 S284 T319 T43 S80 T137 T155 T211 S238 T239	N209	C2H2 zinc fingers: C143-C171 Y169-H191 F197-H219	zinc finger protein (g220643)	MOTIFS BLAST PFAM BLOCKS
34	106	S80 T89 T39 T53		Homeobox: R14-K70	CHOX M product; homeobox protein (g62701)	MOTIFS BLAST BLOCKS PFAM PROFILES SCAN
35	209	S176 T180 S184 T193 S201 S4 T25 S49	N18	bZIP transcription factor: K115-E140	geminin (g3219357)	MOTIFS BLAST PFAM
36	212	S79 S107 T127 T202 S45 S56 S124 T152 Y35	N92	HMG box: M1-Q36	Smarcel-related protein (GI 4321968)	MOTIFS BLAST PFAM
37	359	T329 T50 S125 S224 S230 S235 S344 S31 S215 S312 Y42	N45 N340	C2H2 zinc fingers: F278-C306 Y304-H328 F334-H356	BKLF; CACCC-box binding protein (gl244515)	MOTIFS BLAST BLOCKS PFAM
38	445	S68 T87 S153 S339 S405 S55 T105 S315 S422 Y419	N337 N374 N388	C3HC4 RING fingers: C74-P120 N228-C235	ARI (RING finger) protein (g2058299)	MOTIFS BLAST BLOCKS PFAM
39	433	S283 T44 T57 T123 S136 T185 T220 S239 T268 S313 S330 T105 T109 S125 T216	N169 N206		sKm-BOP2 zinc finger protein (gl809327)	MOTIFS BLAST

TABLE 2 (cont.)

Polypeptide Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequence(s)	Identification/ Homologous Sequence	Analytical Methods and Databases
40	355	T72 T84 T184 S191 T244 S88 T162 T229 T294 S330	N308 N324		Sir2 family protein (g5353746)	MOTIFS BLAST
41	443	T76 T106 S148 T309 S12 T253 S299 S357 T373 T427 Y61 Y114	N366 N425	Myb-like DNA binding domain: D72-F118	ADA2 transcriptional adaptor protein (g170991)	MOTIFS BLAST BLOCKS PFAM
42	164	S37 T55 T64 S83 S22 Y146	N117	mutT domain: V29-L70		PROFILESAN MOTIFS BLOCKS PFAM
43	215	S79 S127 T12 T45		HMG box: M1-Q36	Sry-related protein (g211510)	MOTIFS BLAST PFAM
44	539	T15 S24 S66 S83 T97 T105 T109 S128 T149 S153 S198 T203 T225 T238 T296 S466 Y258	N465	C2H2 zinc fingers: H230-H252 Y258-H280 Y286-H308 Y314-H336 Y342-H364 F370-H392 Y398-H420 Y426-H448 Y482-H504 Y510-H532	C2H2 zinc finger protein (g5757625)	MOTIFS BLAST PFAM BLOCKS
45	182	T59 S112 S120 S100 S139 Y64			Transcriptional regulator (g2621798)	MOTIFS BLAST

TABLE 2 (cont.)

Polypeptide Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequence(s)	Identification/ Homologous Sequence	Analytical Methods and Databases
46	534	S494 S31 S44 S117 T123 S185 S216 S476 S504 S176 S182 S211 T249 S293 S323 S409 T489 Y76 Y285	N29 N39 N250 N351	C2H2 zinc fingers: Y285-H307 Y313-H335 Y341-H363 C369-H391 Y397-H419 Y425-H447 Y453-H475 Y481-H503 Y509-H531	Zinc finger protein (g1373394)	MOTIFS BLAST PFAM BLOCKS
47	206	S5 S7 S40 S45 S46 S100 S144 S26 S107 T148 S185 Y38	N44 N177	Myc-type HLH domain: Q108-R160	Musculin (g3599519)	MOTIFS BLAST PFAM BLOCKS PROFILES SCAN
48	172	T5 S87 S96 S115 T124 S22 T64			KRAB zinc finger protein (g1049295)	MOTIFS BLAST
49	275	S185 S14 S48 T54 S118 T139 T161 T189 T217 Y256	N210 N214 N238 N260	C2H2 zinc fingers: F172-H194 Y200-H222 Y228-H250	Repressor transcriptional factor (g1017722)	MOTIFS BLAST PFAM BLOCKS
50	236	S157 S42 T167 T222 T81 Y213	N40	C3HC4 RING finger: P126-L150	Ariadne-2 RING finger protein (g3445441)	MOTIFS BLAST BLOCKS
51	214	S7 S8 S116 T127 S154 S191 T31 S41 T204	N2	Chromodomain: V113-E134	Nucleoplasmin (g833629)	MOTIFS BLAST BLOCKS

TABLE 2 (cont.)

Polypeptide Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequence(s)	Identification/ Homologous Sequence	Analytical Methods and Databases
52	396	T348 T392 S118 T193 T201 S270 S294 S80 S112 S206 S260 T313 T355 S375 S387	N2	C3HC4 RING finger: C26-C50	Midline 1/ cerebellar isoform 1 RING finger protein (g3462503)	MOTIFS BLAST PFAM BLOCKS PROFILES SCAN
53	486	S29 T58 S155 S239 T292 T379 S146 T271 S425			5'-nucleotidase (g633071)	MOTIFS BLAST
54	555	S432 T502 S68 S195 T199 T226 S315 T379 T441 T534 S170 S248 S282 S291 T327 T336 S391 S422 T481 Y257 Y274 T34 T42 Y48	N25 N66 N246 N364	ATP/GTP binding site (P-loop): A434-T441	Transcription termination factor I (TTF-I) interacting peptide 5 isoform (g2183083)	MOTIFS BLAST
55	61				Putative leucine-rich DNA-binding protein (g555991)	MOTIFS BLAST

TABLE 3

Nucleotide Seq ID NO:	Selected Fragment	Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
56	169-215	Reproductive (0.224) Nervous (0.198) Cardiovascular (0.112)	Cell Proliferative (0.725) Inflammation (0.190)	PBLUESCRIPT
57	551-595	Hematopoietic/Immune (0.240) Reproductive (0.180) Gastrointestinal (0.120)	Cell Proliferative (0.700) Inflammation (0.360)	PBLUESCRIPT
58	541-585	Nervous (0.286) Reproductive (0.286) Cardiovascular (0.214)	Cell Proliferative (0.643) Trauma (0.214)	PBLUESCRIPT
59	109-153	Reproductive (1.000)	Cell Proliferative (1.000) Inflammation (1.000)	PBLUESCRIPT
60	435-479	Hematopoietic/Immune (0.211) Gastrointestinal (0.183) Reproductive (0.183)	Cell Proliferative (0.620) Inflammation (0.338)	PBLUESCRIPT
61	1195-1239	Reproductive (0.248) Cardiovascular (0.174) Nervous (0.157)	Cell Proliferative (0.637) Inflammation (0.256)	PBLUESCRIPT
62	217-261	Reproductive (0.429) Nervous (0.238) Cardiovascular (0.095)	Cell Proliferative (0.667) Inflammation (0.143) Trauma (0.095)	PBLUESCRIPT
63	919-963	Reproductive (0.265) Nervous (0.235) Cardiovascular (0.088)	Cell Proliferative (0.618) Inflammation (0.206)	PSPORT1
64	823-876	Reproductive (0.382) Nervous (0.176) Gastrointestinal (0.118)	Cell Proliferative (0.794)	PSPORT1
65	380-424	Reproductive (0.346) Nervous (0.154) Gastrointestinal (0.135)	Cell Proliferative (0.750) Inflammation (0.231)	PSPORT1

TABLE 3 (cont.)

Nucleotide Seq ID NO:	Selected Fragment	Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
66	757-801	Nervous (0.222) Hematopoietic/Immune (0.167) Reproductive (0.167)	Cell Proliferative (0.778) Inflammation (0.222)	pINCY
67	812-856	Reproductive (0.246) Nervous (0.180) Gastrointestinal (0.148)	Cell Proliferative (0.639) Inflammation (0.246)	pINCY
68	326-370	Reproductive (0.500) Nervous (0.200) Gastrointestinal (0.150)	Cell Proliferative (0.700) Trauma (0.150)	pINCY
69	703-747	Reproductive (0.278) Hematopoietic/Immune (0.204) Nervous (0.148)	Cell Proliferative (0.777) Inflammation (0.222)	pINCY
70	759-803	Reproductive (0.261) Gastrointestinal (0.217) Nervous (0.174)	Cell Proliferative (0.565) Trauma (0.130)	pINCY
71	110-154	Nervous (0.250) Developmental (0.208) Gastrointestinal (0.167)	Cell Proliferative (0.583) Trauma (0.167)	pINCY
72	529-573	Reproductive (0.186) Gastrointestinal (0.168) Hematopoietic/Immune (0.138)	Cell Proliferative (0.700) Inflammation (0.251)	pINCY
73	1784-1828	Reproductive (0.286) Hematopoietic/Immune (0.190) Nervous (0.167)	Cell Proliferative (0.667) Inflammation (0.286)	PSPORT1
74	111-155	Reproductive (0.316) Nervous (0.211) Hematopoietic/Immune (0.158)	Cell Proliferative (0.632) Inflammation (0.211)	PSPORT1
75	543-587	Reproductive (0.258) Nervous (0.206) Gastrointestinal (0.134)	Cell Proliferative (0.608) Inflammation (0.196)	pINCY

TABLE 3 (cont.)

Nucleotide Seq ID NO:	Selected Fragment	Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
76	272-316	Reproductive (0.246) Nervous (0.180) Hematopoietic/Immune (0.148)	Cell Proliferative (0.606) Inflammation (0.279)	pINCY
77	227-271	Hematopoietic/Immune (0.222) Endocrine (0.167) Cardiovascular (0.111)	Cell Proliferative (0.666) Inflammation (0.333)	pINCY
78	487-531	Gastrointestinal (0.375) Reproductive (0.250)	Cell Proliferative (0.500) Inflammation (0.250)	pINCY
79	111-155	Gastrointestinal (0.280) Hematopoietic/Immune (0.240) Reproductive (0.120)	Cell Proliferative (0.640) Inflammation (0.440)	pINCY
80	595-639	Reproductive (0.211) Gastrointestinal (0.158) Urologic (0.158)	Cell Proliferative (0.684) Inflammation (0.263)	pINCY
81	425-469	Reproductive (0.222) Gastrointestinal (0.160) Nervous (0.148)	Cell Proliferative (0.568) Inflammation (0.259)	PSPORT1
82	774-818	Gastrointestinal (0.200) Hematopoietic/Immune (0.200) Nervous (0.200)	Cancer (0.600) Trauma (0.200) Inflammation (0.200)	PBLUESCRIPT
83	517-561	Nervous (0.526) Reproductive (0.132) Cardiovascular (0.105)	Cancer (0.342) Fetal (0.158) Inflammation (0.158)	PBLUESCRIPT
84	1944-1988	Nervous (0.250) Reproductive (0.188) Endocrine (0.125)	Cancer (0.438) Fetal (0.250) Trauma (0.250)	PSPORT1
85	1027-1071	Reproductive (0.219) Nervous (0.206) Hematopoietic/Immune (0.116)	Cancer (0.458) Inflammation (0.232) Fetal (0.181)	PSPORT1

TABLE 3 (cont.)

Nucleotide Seq ID NO:	Selected Fragment	Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
86	658-702	Reproductive (0.227) Hematopoietic/Immune (0.182) Gastrointestinal (0.167)	Cancer (0.424) Inflammation (0.318) Fetal (0.167)	PT7T3
87	488-532	Nervous (0.200) Reproductive (0.200) Musculoskeletal (0.120)	Cancer (0.320) Fetal (0.320) Inflammation (0.320)	pINCY
88	379-423	Cardiovascular (0.250) Nervous (0.250) Reproductive (0.250)	Cancer (0.417) Fetal (0.167) Neurological (0.167)	pINCY
89	632-676	Reproductive (0.417) Cardiovascular (0.167) Gastrointestinal (0.167)	Cancer (0.333) Fetal (0.167) Inflammation (0.167)	pINCY
90	258-302	Reproductive (0.294) Nervous (0.137) Hematopoietic/Immune (0.118)	Cancer (0.569) Fetal (0.431) Inflammation (0.176)	pINCY
91	433-477	Reproductive (0.750) Nervous (0.250)	Cancer (0.500) Inflammation (0.500)	PSPORT1
92	542-586	Gastrointestinal (0.273) Hematopoietic/Immune (0.273) Developmental (0.182)	Cancer (0.455) Inflammation (0.364) Fetal (0.182)	pINCY
93	218-262	Reproductive (0.272) Nervous (0.204) Cardiovascular (0.126)	Cancer (0.447) Inflammation (0.214) Fetal (0.155)	PSPORT1
94	541-585	Reproductive (0.273) Nervous (0.250) Cardiovascular (0.159)	Cancer (0.364) Fetal (0.205) Inflammation (0.205)	PSPORT1
95	111-155	Reproductive (0.250) Gastrointestinal (0.173) Nervous (0.154)	Cancer (0.481) Fetal (0.231) Inflammation (0.212)	PSPORT1
96	597-641	Reproductive (0.261) Cardiovascular (0.217) Nervous (0.130)	Cancer (0.391) Fetal (0.304) Inflammation (0.130)	PSPORT1

TABLE 3 (cont.)

Nucleotide Seq ID NO:	Selected Fragment	Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
97	434-478	Cardiovascular (0.222) Endocrine (0.222) Gastrointestinal (0.222)	Cancer (0.667) Fetal (0.111) Neurological (0.111)	PSPORT1
98	218-247 920-964	Reproductive (0.333) Gastrointestinal (0.129) Hematopoietic/Immune (0.118)	Cancer (0.559) Inflammation (0.204) Fetal (0.183)	pINCY
99	327-371	Gastrointestinal (0.211) Reproductive (0.211) Cardiovascular (0.158)	Cancer (0.421) Fetal (0.316) Inflammation (0.158)	pINCY
100	596-625	Reproductive (0.230) Nervous (0.164) Gastrointestinal (0.131)	Cancer (0.590) Inflammation (0.246) Fetal (0.082)	PSPORT
101	487-531	Cardiovascular (0.235) Reproductive (0.235) Hematopoietic/Immune (0.176)	Cancer (0.588) Inflammation (0.176) Trauma (0.118)	pINCY
102	218-247 542-586	Gastrointestinal (0.241) Hematopoietic/Immune (0.207) Cardiovascular (0.138)	Cancer (0.448) Fetal (0.276) Inflammation (0.276)	pINCY
103	219-263	Reproductive (0.500) Cardiovascular (0.250) Hematopoietic/Immune (0.250)	Cancer (0.500) Inflammation (0.250) Trauma (0.250)	pINCY
104	111-140 327-371	Hematopoietic/Immune (0.286) Nervous (0.238) Reproductive (0.143)	Cancer (0.333) Fetal (0.286) Inflammation (0.286)	pINCY
105	243-281	Musculoskeletal (0.286) Nervous (0.286) Gastrointestinal (0.143)	Inflammation (0.429) Fetal (0.286) Cancer (0.286)	pINCY
106	271-315	Nervous (0.800) Reproductive (0.100) Cardiovascular (0.100)	Cancer (0.400) Inflammation (0.200) Trauma (0.200)	pINCY

TABLE 3 (cont.)

Nucleotide Seq ID NO:	Selected Fragment	Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
107	489-533	Cardiovascular (0.364) Gastrointestinal (0.182) Reproductive (0.182)	Cancer (0.273) Trauma (0.273) Inflammation (0.182)	pINCY
108	156-200	Nervous (0.256) Reproductive (0.256) Hematopoietic/Immune (0.128)	Cancer (0.465) Fetal (0.291) Inflammation (0.186)	pINCY
109	1459-1503	Cardiovascular (0.250) Hematopoietic/Immune (0.250) Nervous (0.167)	Inflammation (0.417) Cancer (0.333) Trauma (0.167)	PSPORT1
110	164-208	Nervous (1.000)	Neurological (1.000)	pINCY

TABLE 4

Nucleotide SEQ ID NO:	Library	Library Comment
56	SPLNFET0 1	Library was constructed at Stratagene, using RNA isolated from a pool of fetal spleen tissue. Following vector packaging, 2x10 ⁶ primary clones were then amplified to stabilize the library for long-term storage. Amplification may significantly skew sequence abundances.
57	SYNORAB0 1	Library was constructed using RNA isolated from the synovial membrane tissue of a 68-year-old Caucasian female with rheumatoid arthritis.
58	KIDNNOT0 1	Library was constructed using RNA isolated from the kidney tissue of a 64-year-old Caucasian female, who died from an intracranial bleed. Patient history included rheumatoid arthritis and tobacco use.
59	PLACNOB0 1	Library was constructed using RNA isolated from placenta.
60	HNT2RAT0 1	Library was constructed at Stratagene (STR937231), using RNA isolated from the hNT2 cell line (derived from a human teratocarcinoma that exhibited properties characteristic of a committed neuronal precursor). Cells were treated with retinoic acid for 24 hours.
61	EOSIHET0 2	Library was constructed using RNA isolated from peripheral blood cells apheresed from a 48-year-old Caucasian male. Patient history included hypereosinophilia. The cell population was determined to be greater than 77% eosinophils by Wright's staining.
62	HNT2AGT0 1	Library was constructed at Stratagene (STR937233), using RNA isolated from the hNT2 cell line (derived from a human teratocarcinoma that exhibited properties characteristic of a committed neuronal precursor). Cells were treated with retinoic acid for 5 weeks and with mitotic inhibitors for two weeks and allowed to mature for an additional 4 weeks in conditioned medium.
63	PROSNOT0 2	Library was constructed using RNA isolated from the diseased prostate tissue removed from a 50-year-old Caucasian male during a retropubic prostatectomy. Pathology indicated adenofibromatous hyperplasia was present. Pathology for the associated tumor tissue indicated adenocarcinoma Gleason grade 3+3. Patient history included dysuria, carcinoma in situ of prostate, coronary atherosclerosis, and hyperlipidemia.
64	COUNTUT0 2	Library was constructed using RNA isolated from colon tumor tissue removed from a 75-year-old Caucasian male during a hemicolectomy. Pathology indicated invasive grade 3 adenocarcinoma arising in a tubulovillous adenoma, which was distal to the ileocecal valve in the cecum. The tumor penetrated deeply into the muscularis propria but not through it.

TABLE 4 (cont.)

Nucleotide SEQ ID NO:	Library	Library Comment
65	KIDNTUT0 1	Library was constructed using RNA isolated from the kidney tumor tissue removed from an 8-month-old female during nephroureterectomy. Pathology indicated Wilms' tumor (nephroblastoma), which involved 90 percent of the renal parenchyma. Prior to surgery, the patient was receiving heparin anticoagulant therapy.
66	THYRNOT0 3	Library was constructed using RNA isolated from thyroid tissue removed from the left thyroid of a 28-year-old Caucasian female during a complete thyroidectomy. Pathology indicated a small nodule of adenomatous hyperplasia present in the left thyroid. Pathology for the associated tumor tissue indicated dominant follicular adenoma, forming a well-encapsulated mass in the left thyroid.
67	BLADTUT0 4	Library was constructed using RNA isolated from bladder tumor tissue removed from a 60-year-old Caucasian male during a radical cystectomy, prostatectomy, and vasectomy. Pathology indicated grade 3 transitional cell carcinoma in the left bladder wall. Carcinoma in-situ was identified in the dome and trigone. Patient history included tobacco use. Family history included type I diabetes, a malignant neoplasm of the stomach, atherosclerotic coronary artery disease, and an acute myocardial infarction.
68	PROSNOT1 5	Library was constructed using RNA isolated from diseased prostate tissue removed from a 66-year-old Caucasian male during radical prostatectomy and regional lymph node excision. Pathology indicated adenofibromatous hyperplasia. Pathology for the associated tumor tissue indicated an adenocarcinoma (Gleason grade 2+3). The patient presented with elevated prostate specific antigen (PSA). Family history included prostate cancer, secondary bone cancer, and benign hypertension.
69	BRSTTUT0 8	Library was constructed using RNA isolated from breast tumor tissue removed from a 45-year-old Caucasian female during unilateral extended simple mastectomy. Pathology indicated invasive nuclear grade 2-3 adenocarcinoma, ductal type, with 3 of 23 lymph nodes positive for metastatic disease. Greater than 50% of the tumor volume was in situ, both comedo and non-comedo types. Immunostains were positive for estrogen/progesterone receptors, and uninvolved tissue showed proliferative changes. The patient concurrently underwent a total abdominal hysterectomy. Patient history included valvuloplasty of mitral valve without replacement, rheumatic mitral insufficiency, and rheumatic heart disease. Family history included acute myocardial infarction, atherosclerotic coronary artery disease, and type II diabetes.

TABLE 4 (cont.)

Nucleotide SEQ ID NO:	Library	Library Comment
70	PROSNOT1 9	Library was constructed using RNA isolated from diseased prostate tissue removed from a 59-year-old Caucasian male during a radical prostatectomy with regional lymph node excision. Pathology indicated adenofibromatous hyperplasia. Pathology for the associated tumor tissue indicated an adenocarcinoma (Gleason grade 3+3). The patient presented with elevated prostate-specific antigen (PSA). Patient history included colon diverticuli, asbestosis, and thrombophlebitis. Previous surgeries included a partial colectomy. Family history included benign hypertension, multiple myeloma, hyperlipidemia and rheumatoid arthritis.
71	THP1NOT0 3	Library was constructed using RNA isolated from untreated THP-1 cells. THP-1 (ATCC TIB 202) is a human promonocyte line derived from the peripheral blood of a 1-year-old Caucasian male with acute monocytic leukemia (ref: Int. J. Cancer (1980) 26:171).
72	THP1NOT0 3	Library was constructed using RNA isolated from untreated THP-1 cells. THP-1 (ATCC TIB 202) is a human promonocyte line derived from the peripheral blood of a 1-year-old Caucasian male with acute monocytic leukemia (ref: Int. J. Cancer (1980) 26:171).
73	HIPOAZT0 1	Library was constructed from RNA isolated from diseased hippocampus tissue removed from the brain of a 74-year-old Caucasian male who died from Alzheimer's disease.
74	HIPOAZT0 1	Library was constructed from RNA isolated from diseased hippocampus tissue removed from the brain of a 74-year-old Caucasian male who died from Alzheimer's disease.
75	BRSTNOT1 3	Library was constructed using RNA isolated from breast tissue removed from the left medial lateral breast of a 36-year-old Caucasian female during bilateral simple mastectomy and total breast reconstruction. Pathology indicated benign breast tissue. Patient history included a breast neoplasm, depressive disorder, hyperlipidemia, chronic stomach ulcer, and an ectopic pregnancy. Family history included myocardial infarction, cerebrovascular disease, atherosclerotic coronary artery disease, hyperlipidemia, skin cancer, breast cancer, depressive disorder, esophageal cancer, bone cancer, Hodgkin's lymphoma, bladder cancer, and heart condition.
76	NPOLNOT0 1	Library was constructed using RNA isolated from nasal polyp tissue removed from a 78-year-old Caucasian male during a nasal polypectomy. Pathology indicated a nasal polyp and striking eosinophilia. Patient history included asthma and nasal polyps.

TABLE 4 (cont.)

Nucleotide SEQ ID NO:	Library	Library Comment
77	ADRENOT0 9	Library was constructed using RNA isolated from left adrenal gland tissue removed from a 43-year-old Caucasian male during nephroureterectomy, regional lymph node excision, and unilateral left adrenalectomy. Pathology indicated no diagnostic abnormalities of the adrenal gland. Pathology for the associated tumor tissue indicated a grade 2 renal cell carcinoma mass in the posterior lower pole of the left kidney with invasion into the renal pelvis.
78	SPLNOT1 1	Library was constructed using RNA isolated from diseased spleen tissue removed from a 14-year-old Asian male during a total splenectomy. Pathology indicated changes consistent with idiopathic thrombocytopenic purpura. The patient presented with bruising.
79	CONCNOT0 1	Library was constructed using RNA isolated from chest wall soft tissue removed from a 63-year-old Caucasian male during a chest wall lesion destruction. Pathology indicated surgical margins were free of tumor. Pathology for the associated tumor tissue indicated invasive grade 3 adenocarcinoma, forming a mass that extended through the visceral pleura to involve parietal pleura. Patient history included MEN (multiple endocrine neoplasia) syndrome type I, abnormal secretion of gastrin, alcohol and tobacco abuse, calcium metabolism disease, chronic stomach ulcer with hemorrhage, lung cancer, and calculus of the kidney. Family history included prostate cancer, benign hypertension, stroke, atherosclerotic coronary artery disease, type II diabetes, hyperlipidemia, and cancer of an unspecified location.
80	TONSNOT0 3	Library was constructed using RNA isolated from diseased left tonsil tissue removed from a 6-year-old Caucasian male during adenotonsillectomy. Pathology indicated reactive lymphoid hyperplasia, bilaterally. Family history included benign hypertension, myocardial infarction, and atherosclerotic coronary artery disease.
81	LUNGNOT0 3	This normalized library was constructed from 2.56×10^6 independent clones from a lung tissue library. RNA was made from lung tissue removed from the left lobe a 58-year-old Caucasian male during a segmental lung resection. Pathology for the associated tumor tissue indicated a metastatic grade 3 (of 4) osteosarcoma. Patient history included soft tissue cancer, secondary cancer of the lung, prostate cancer, and an acute duodenal ulcer with hemorrhage. Patient also received radiation therapy to the retroperitoneum. Family history included prostate cancer, breast cancer, and acute leukemia. The normalization and hybridization conditions were adapted from Soares et al., PNAS (1994) 91:9228; Swaroop et al., NAR (1991) 19:1954; and Ronaldo et al., Genome Research (1996) 6:791.

TABLE 4 (cont.)

Nucleotide SEQ ID NO:	Library	Library Comment
82	BMARNOT0 2	The library was constructed using Clontech RNA isolated from the bone marrow of 24 male and female Caucasian donors, 16 to 70 years old.
83	SINTNOT0 2	The library was constructed using RNA isolated from the small intestine of a 55-year-old Caucasian female, who died from a subarachnoid hemorrhage. Serologies were positive for cytomegalovirus (CMV).
84	CRBLNOT0 1	The library was constructed using RNA isolated from the cerebellum tissue of a 69-year-old Caucasian male who died from chronic obstructive pulmonary disease. Patient history included myocardial infarction, hypertension, and osteoarthritis.
85	BRSTNOT0 3	The library was constructed using RNA isolated from diseased breast tissue removed from a 54-year-old Caucasian female during a bilateral radical mastectomy. Pathology for the associated tumor tissue indicated residual invasive grade 3 mammary ductal adenocarcinoma. Patient history included kidney infection and condyloma acuminatum. Family history included benign hypertension, hyperlipidemia and a malignant neoplasm of the colon.
86	BEPINOT0 1	The normalized bronchial epithelium library was constructed from 5.12 million independent clones from a bronchial epithelium library. RNA was isolated from a bronchial epithelium primary cell line derived from a 54-year-old Caucasian male. The normalization and hybridization conditions were adapted from Soares et al., PNAS (1994) 91:9228, using a 24-hour reannealing hybridization period.
87	THYRNOT0 3	The library was constructed using RNA isolated from thyroid tissue removed from the left thyroid of a 28-year-old Caucasian female during a complete thyroidectomy. Pathology indicated a small nodule of adenomatous hyperplasia present in the left thyroid. Pathology for the associated tumor tissue indicated dominant follicular adenoma, forming a well-encapsulated mass in the left thyroid.
88	COLNFETO 2	The library was constructed using RNA isolated from the colon tissue of a Caucasian female fetus who died at 20 weeks' gestation.
89	BLADNOT0 3	The library was constructed using RNA isolated from bladder tissue removed from an 80-year-old Caucasian female during a radical cystectomy and lymph node excision. Pathology for the associated tumor tissue indicated grade 3 invasive transitional cell carcinoma. Patient history included malignant neoplasm of the uterus, atherosclerosis, and atrial fibrillation. Family history included acute renal failure, osteoarthritis, and atherosclerosis.

TABLE 4 (cont.)

Nucleotide SEQ ID NO:	Library	Library Comment
90	COLNNOT2 3	The library was constructed using RNA isolated from diseased colon tissue removed from a 16-year-old Caucasian male during a total colectomy with abdominal/perineal resection. Pathology indicated gastritis and pancolitis consistent with the acute phase of ulcerative colitis. Inflammation was more severe in the transverse colon with inflammation confined to the mucosa. The ascending and sigmoid colon was mildly involved. Family history included irritable bowel syndrome.
91	BRSTNOT0 4	The library was constructed using RNA isolated from breast tissue removed from a 62-year-old East Indian female during a unilateral extended simple mastectomy. Pathology for the associated tumor tissue indicated an invasive grade 3 ductal carcinoma. Patient history included benign hypertension, hyperlipidemia, and hematuria. Family history included cerebrovascular and cardiovascular disease, hyperlipidemia, and liver cancer.
92	LIVRFETO 2	The library was constructed using RNA isolated from liver tissue removed from a Caucasian female fetus who died at 20 weeks' gestation. Family history included seven days of erythromycin treatment for bronchitis in the mother during the first trimester.
93	BEPINOT0 1	The library was constructed using RNA isolated from a bronchial epithelium primary cell line derived from a 54-year-old Caucasian male.
94	BRAITUTO 2	The library was constructed using RNA isolated from brain tumor tissue removed from the frontal lobe of a 58-year-old Caucasian male during excision of a cerebral meningeal lesion. Pathology indicated a grade 2 metastatic hypernephroma. Patient history included a grade 2 renal cell carcinoma, insomnia, and chronic airway obstruction. Family history included a malignant neoplasm of the kidney.
95	BRAITUTO 3	The library was constructed using RNA isolated from brain tumor tissue removed from the left frontal lobe of a 17-year-old Caucasian female during excision of a cerebral meningeal lesion. Pathology indicated a grade 4 fibrillary giant and small-cell astrocytoma. Family history included benign hypertension and cerebrovascular disease.
96	BRSTTUTO 2	The library was constructed using RNA isolated from breast tumor tissue removed from a 54-year-old Caucasian female during a bilateral radical mastectomy with reconstruction. Pathology indicated residual invasive grade 3 mammary ductal adenocarcinoma. The remaining breast parenchyma exhibited proliferative fibrocystic changes without atypia. One of 10 axillary lymph nodes had metastatic tumor. Patient history included kidney infection and condyloma acuminatum. Family history included benign hypertension, hyperlipidemia, and a malignant colon neoplasm.

TABLE 4 (cont.)

Nucleotide SEQ ID NO:	Library	Library Comment
97	BRSTTUT0 2	The library was constructed using RNA isolated from breast tumor tissue removed from a 54-year-old Caucasian female during a bilateral radical mastectomy with reconstruction. Pathology indicated residual invasive grade 3 mammary ductal adenocarcinoma. The remaining breast parenchyma exhibited proliferative fibrocystic changes without atypia. One of 10 axillary lymph nodes had metastatic tumor. Patient history included kidney infection and condyloma acuminatum. Family history included benign hypertension, hyperlipidemia, and a malignant colon neoplasm.
98	BRSTNOT0 7	The library was constructed using RNA isolated from diseased breast tissue removed from a 43-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology indicated mildly proliferative fibrocystic changes with epithelial hyperplasia, papillomatosis, and duct ectasia. Pathology for the associated tumor tissue indicated invasive grade 4, nuclear grade 3 mammary adenocarcinoma with extensive comedo necrosis. Family history included epilepsy, cardiovascular disease, and type II diabetes.
99	BRAINOT0 9	The library was constructed using RNA isolated from brain tissue removed from a Caucasian male fetus who died at 23 weeks' gestation.
100	THP1AZS0 8	The library was constructed using RNA isolated from 5.76 million clones from a 5-aza-2'-deoxycytidine treated THP-1 cell library. The library was subjected to subtractive hybridization using 5 million clones from an untreated THP-1 cell library. Hybridization conditions were adapted from Swaroop et al., NAR (1991) 19:1954; and Bonaldo et al., Genome Research (1996) 6:791. THP-1 (ATCC TIB 202) is a human promonocyte cell line derived from peripheral blood of a 1-year-old Caucasian male with acute monocytic leukemia.
101	LUNGUT1 2	The library was constructed using RNA isolated from tumorous lung tissue removed from a 70-year-old Caucasian female during a lung lobectomy of the left upper lobe. Pathology indicated grade 3 (of 4) adenocarcinoma and vascular invasion. Patient history included tobacco abuse, depressive disorder, anxiety state, and skin cancer. Family history included cerebrovascular disease, congestive heart failure, colon cancer, depressive disorder, and primary liver.
102	HEAONOT0 5	The library was constructed using RNA isolated from aortic tissue removed from a 17-year-old Hispanic female who died from a gunshot wound.
103	HEAONOT0 5	The library was constructed using RNA isolated from aortic tissue removed from a 17-year-old Hispanic female who died from a gunshot wound.

TABLE 4 (cont.)

Nucleotide SEQ ID NO:	Library	Library Comment
104	EPIGNOTO 1	The library was constructed using RNA isolated from epiglottic tissue removed from a 71-year-old male during laryngectomy with right parathyroid biopsy. Pathology for the associated tumor tissue indicated recurrent grade 1 papillary thyroid carcinoma.
105	CONCNOTO 1	The library was constructed using RNA isolated from chest wall soft tissue removed from a 63-year-old Caucasian male during a chest wall lesion destruction. Pathology for the associated tumor tissue indicated invasive grade 3 adenocarcinoma forming a mass that extended through the visceral pleura to involve parietal pleura. Patient history included multiple endocrine neoplasia syndrome type I, abnormal secretion of gastrin, alcohol and tobacco abuse, calcium metabolism disease, chronic stomach ulcer with hemorrhage, lung cancer, and calculus of the kidney. Family history included prostate cancer, benign hypertension, stroke, atherosclerotic coronary artery disease, type II diabetes, hyperlipidemia, and an unspecified cancer.
106	BRONNOTO 1	The library was constructed using RNA isolated from bronchial tissue removed from a 15-year-old Caucasian male.
107	BRONNOTO 1	The library was constructed using RNA isolated from bronchial tissue removed from a 15-year-old Caucasian male.
108	LIVRNOTO 3	The library was constructed using RNA isolated from liver tissue removed from a Caucasian male fetus who died from Patau's syndrome (trisomy 13) at 20 weeks' gestation.
109	LUNGNONO 3	The normalized library was constructed from 2.56 million independent clones from a lung tissue library. RNA was isolated from lung tissue removed from the left lobe a 58-year-old Caucasian male during a segmental lung resection. Pathology for the associated tumor tissue indicated a metastatic grade 3 (of 4) osteosarcoma. Patient history included soft tissue cancer, secondary cancer of the lung, prostate cancer, acute duodenal ulcer with hemorrhage, and radiation therapy to the retroperitoneum. Family history included prostate cancer, breast cancer, and acute leukemia. The normalization and hybridization conditions were adapted from Soares et al., PNAS (1994) 91:9228; Swaroop et al., NAR (1991) 19:1954; and Bonaldo et al., Genome Research (1996) 6:791.
110	BRAIHCTO 2	The library was constructed using RNA isolated from diseased choroid plexus tissue removed from the brain of a 57-year-old Caucasian male who died from a cerebrovascular accident. Patient history included Huntington's disease and emphysema.

Table 5

Program	Description	Reference	Parameter Threshold
ABI FACTURA	A program that removes vector sequences and masks ambiguous bases in nucleic acid sequences.	Perkin-Elmer Applied Biosystems, Foster City, CA.	
ABI/PARACEL FDF	A Fast Data Finder useful in comparing and annotating amino acid or nucleic acid sequences.	Perkin-Elmer Applied Biosystems, Foster City, CA; Paracel Inc., Pasadena, CA.	Mismatch <50%
ABI AutoAssembler	A program that assembles nucleic acid sequences.	Perkin-Elmer Applied Biosystems, Foster City, CA.	
BLAST	A Basic Local Alignment Search Tool useful in sequence similarity search for amino acid and nucleic acid sequences. BLAST includes five functions: blastp, blastn, blastx, tblastn, and tblastx.	Altschul, S.F. et al. (1990) J. Mol. Biol. 215:403-410; Altschul, S.F. et al. (1997) Nucleic Acids Res. 25: 3389-3402.	ESTs: Probability value= 1.0E-8 or less Full Length sequences: Probability value= 1.0E-10 or less
FASTA	A Pearson and Lipman algorithm that searches for similarity between a query sequence and a group of sequences of the same type. FASTA comprises at least five functions: fasta, tfasta, fastx, tfastx, and ssearch.	Pearson, W.R. and D.J. Lipman (1988) Proc. Natl. Acad. Sci. 85:2444-2448; Pearson, W.R. (1990) Methods Enzymol. 183: 63-98; and Smith, T.F. and M. S. Waterman (1981) Adv. Appl. Math. 2:482-489.	ESTs: fasta E value= 1.06E-6 Assembled ESTs: fasta Identity= 95% or greater and Match length=200 bases or greater. fastx E value=1.0E-8 or less Full Length sequences: fastx score= 100 or greater
BLIMPS	A BLOCKS IMPROVED Searcher that matches a sequence against those in BLOCKS, PRINTS, DOMO, PRODOM, and PFAM databases to search for gene families, sequence homology, and structural fingerprint regions.	Henikoff, S and J.G. Henikoff, Nucl. Acid Res., 19:6565-72, 1991. J.G. Henikoff and S. Henikoff (1996) Methods Enzymol. 266:88-105; and Attwood, T.K. et al. (1997) J. Chem. Inf. Comput. Sci. 37: 417-424.	Score= 1000 or greater; Ratio of Score/Strength = 0.75 or larger; and, if applicable, Probability value= 1.0E-3 or less
HIMMER	An algorithm for searching a query sequence against hidden Markov model (HMM)-based databases of protein family consensus sequences, such as PFAM.	Krogh, A. et al. (1994) J. Mol. Biol., 235:1501-1531; Sonnhammer, E.L.L. et al. (1988) Nucleic Acids Res. 26:320-322.	Score= 10-50 bits for PFAM hits, depending on individual protein families

Table 5 (cont.)

Program	Description	Reference	Parameter Threshold
ProfileScan	An algorithm that searches for structural and sequence motifs in protein sequences that match sequence patterns defined in Prosite.	Gribskov, M. et al. (1988) CABIOS 4:61-66; Gribskov, et al. (1989) Methods Enzymol. 183:146-159; Bairoch, A. et al. (1997) Nucleic Acids Res. 25: 217-221.	Normalized quality score > GCG-specified "HIGH" value for that particular Prosite motif. Generally, score=1.4-2.1.
Phred	A base-calling algorithm that examines automated sequencer traces with high sensitivity and probability.	Ewing, B. et al. (1998) Genome Res. 8:175-185; Ewing, B. and P. Green (1998) Genome Res. 8:186-194.	
Phrap	A Phils Revised Assembly Program including SWAT and CrossMatch, programs based on efficient implementation of the Smith-Waterman algorithm, useful in searching sequence homology and assembling DNA sequences.	Smith, T.F. and M. S. Waterman (1981) Adv. Appl. Math. 2:482-489; Smith, T.F. and M. S. Waterman (1981) J. Mol. Biol. 147:195-197; and Green, P., University of Washington, Seattle, WA.	Score= 120 or greater; Match length= 56 or greater
Consed	A graphical tool for viewing and editing Phrap assemblies	Gordon, D. et al. (1998) Genome Res. 8:195-202.	
SPScan	A weight matrix analysis program that scans protein sequences for the presence of secretory signal peptides.	Nielson, H. et al. (1997) Protein Engineering 10:1-6; Claverie, J.M. and S. Audic (1997) CABIOS 12: 431-439.	Score=3.5 or greater
Motifs	A program that searches amino acid sequences for patterns that matched those defined in Prosite.	Bairoch et al. <u>supra</u> ; Wisconsin Package Program Manual, version 9, page M51-59, Genetics Computer Group, Madison, WI.	

What is claimed is:

1. An isolated polypeptide comprising:
 - a) an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID
5 NO:3-5, SEQ ID NO:7-14, SEQ ID NO:16-31, SEQ ID NO:33-34, SEQ ID NO:36-40, SEQ ID
NO:42-48, SEQ ID NO:50-55.
 - b) a naturally occurring amino acid sequence having at least 90% sequence identity to an
amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3-5, SEQ ID
NO:7-14, SEQ ID NO:16-31, SEQ ID NO:33-34, SEQ ID NO:36-40, SEQ ID NO:42-48, SEQ ID
10 NO:50-55,
 - c) a biologically active fragment of an amino acid sequence selected from the group
consisting of SEQ ID NO:1, SEQ ID NO:3-5, SEQ ID NO:7-14, SEQ ID NO:16-31, SEQ ID NO:33-
34, SEQ ID NO:36-40, SEQ ID NO:42-48, SEQ ID NO:50-55, or
 - d) an immunogenic fragment of an amino acid sequence selected from the group consisting
15 of SEQ ID NO:1, SEQ ID NO:3-5, SEQ ID NO:7-14, SEQ ID NO:16-31, SEQ ID NO:33-34, SEQ ID
NO:36-40, SEQ ID NO:42-48, SEQ ID NO:50-55.
2. An isolated polypeptide of claim 1, having an amino acid sequence selected from the
group consisting of SEQ ID NO:1, SEQ ID NO:3-5, SEQ ID NO:7-14, SEQ ID NO:16-31, SEQ ID
20 NO:33-34, SEQ ID NO:36-40, SEQ ID NO:42-48, SEQ ID NO:50-55.
3. An isolated polynucleotide encoding a polypeptide of claim 1.
4. An isolated polynucleotide of claim 3, having a sequence selected from the group
25 consisting of SEQ ID NO:56-110.
5. A recombinant polynucleotide comprising a promoter sequence operably linked to a
polynucleotide of claim 3.
- 30 6. A cell transformed with a recombinant polynucleotide of claim 5.
7. A transgenic organism comprising a polynucleotide of claim 5.
8. A method for producing a polypeptide of claim 1, the method comprising:
35 a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said

cell is transformed with a recombinant polynucleotide, and said recombinant polynucleotide comprises a promoter sequence operably linked to a polynucleotide encoding the polypeptide of claim 1, and

b) recovering the polypeptide so expressed.

5

9. An isolated antibody which specifically binds to a polypeptide of claim 1.

10. An isolated polynucleotide comprising:

10

a) a polynucleotide sequence selected from the group consisting of SEQ ID NO:56-110,

b) a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:56-110,

c) a polynucleotide sequence complementary to a), or

d) a polynucleotide sequence complementary to b).

15

11. An isolated polynucleotide comprising at least 60 contiguous nucleotides of a polynucleotide of claim 10.

12. A method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 10, the method comprising:

a) hybridizing the sample with a probe comprising at least 16 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide, and

b) detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.

13. A method of claim 12, wherein the probe comprises at least 30 contiguous nucleotides.

30

14. A method of claim 12, wherein the probe comprises at least 60 contiguous nucleotides.

15. A pharmaceutical composition comprising an effective amount of a polypeptide of claim 1 and a pharmaceutically acceptable excipient.

35

16. A method of treating a disease or condition associated with decreased expression of

functional NuABP, comprising administering to a patient in need of such treatment the pharmaceutical composition of claim 15.

17. A method for screening a compound for effectiveness as an agonist of a polypeptide of claim 1, the method comprising:
- a) exposing a sample comprising a polypeptide of claim 1 to a compound, and
 - b) detecting agonist activity in the sample.

18. A pharmaceutical composition comprising an agonist compound identified by a method of claim 17 and a pharmaceutically acceptable excipient.

19. A method of treating a disease or condition associated with decreased expression of functional NuABP, comprising administering to a patient in need of such treatment a pharmaceutical composition of claim 18.

15

20. A method for screening a compound for effectiveness as an antagonist of a polypeptide of claim 1, the method comprising:
- a) exposing a sample comprising a polypeptide of claim 1 to a compound, and
 - b) detecting antagonist activity in the sample.

20

21. A pharmaceutical composition comprising an antagonist compound identified by a method of claim 20 and a pharmaceutically acceptable excipient.

22. A method for treating a disease or condition associated with overexpression of functional NuABP, comprising administering to a patient in need of such treatment a pharmaceutical composition of claim 21.

25

23. A method for screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 4, the method comprising:
- a) exposing a sample comprising the target polynucleotide to a compound, and
 - b) detecting altered expression of the target polynucleotide.

30

SEQUENCE LISTING

<110> INCYTE PHARMACEUTICALS, INC.
 TANG, Y. Tom
 LAL, Preeti
 HILLMAN, Jennifer L.
 YUE, Henry
 AZIMZAI, Yalda
 LU, Aina M.D.
 BAUGHN, Mariah R.
 TRAN, Bao
 SHIH, Leo L.
 AU-YOUNG, Janice

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<140> To Be Assigned
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 <151> 1999-01-29; 1999-01-29

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2/91

SUBSTITUTE SHEET (RULE 26)

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				410					415					420	
Ala	His	Phe	His	Ile	His	Gln	Arg	Val	His	Thr	Gly	Glu	Lys	Pro	
				425					430					435	
Tyr	Lys	Cys	Asp	Val	Cys	Gly	Lys	Gly	Phe	Ser	His	Asn	Ser	Pro	
				440					445					450	
Leu	Ile	Cys	His	Arg	Arg	Val	His	Thr	Gly	Glu	Lys	Pro	Tyr	Lys	
				455					460					465	
Cys	Glu	Ala	Cys	Gly	Lys	Gly	Phe	Thr	Arg	Asn	Thr	Asp	Leu	His	
				470					475					480	
Ile	His	Phe	Arg	Val	His	Thr	Gly	Glu	Lys	Pro	Tyr	Lys	Cys	Lys	
				485					490					495	
Glu	Cys	Gly	Lys	Gly	Phe	Ser	Gln	Ala	Ser	Asn	Leu	Gln	Val	His	
				500					505					510	
Gln	Asn	Val	His	Thr	Gly	Glu	Lys	Arg	Phe	Lys	Cys	Glu	Thr	Cys	
				515					520					525	
Gly	Lys	Gly	Phe	Ser	Gln	Ser	Ser	Lys	Leu	Gln	Thr	His	Gln	Arg	

<400> 8														
Met	Leu	Ser	Gly	Arg	Leu	Val	Leu	Gly	Leu	Val	Ser	Met	Ala	Gly
1				5					10					15
Arg	Val	Cys	Leu	Cys	Gln	Gly	Ser	Ala	Gly	Ser	Gly	Ala	Ile	Gly
				20					25					30
Pro	Val	Glu	Ala	Ala	Ile	Arg	Thr	Lys	Leu	Glu	Glu	Ala	Leu	Ser
				35					40					45
Pro	Glu	Val	Leu	Glu	Leu	Arg	Asn	Glu	Ser	Gly	Gly	His	Ala	Val
				50					55					60
Pro	Pro	Gly	Ser	Glu	Thr	His	Phe	Arg	Val	Ala	Val	Val	Ser	Ser
				65					70					75
Arg	Phe	Glu	Gly	Leu	Ser	Pro	Leu	Gln	Arg	His	Arg	Leu	Val	His

	80		85		90
Ala	Ala	Leu	Ala	Glu	Glu
		Leu	Gly	Gly	Pro
				Val	His
				Ala	Leu
					Ala
	95			100	
Ile	Gln	Ala	Arg	Thr	Pro
		Ala	Gln	Trp	Arg
				Glu	Asn
				Ser	Gln
					Leu
	110			115	
Asp	Thr	Ser	Pro	Pro	Cys
		Leu	Gly	Gly	Asn
				Lys	Lys
				Thr	Leu
					Gly
	125			130	
Thr	Pro				

<210> 9
 <211> 230
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 615200CD1

<400> 9
 Met Val Gly Ala Gly Ile Ser Thr Pro Ser Gly Ile Pro Asp Phe
 1 5 10 15
 Arg Ser Pro Gly Ser Gly Leu Tyr Ser Asn Leu Gln Gln Tyr Asp
 20 25 30
 Leu Pro Tyr Pro Glu Ala Ile Phe Glu Leu Pro Phe Phe Phe His
 35 40 45
 Asn Pro Lys Pro Phe Phe Thr Leu Ala Lys Glu Leu Tyr Pro Gly
 50 55 60
 Asn Tyr Lys Pro Asn Ile Thr His Tyr Phe Leu Arg Leu Leu His
 65 70 75
 Asp Lys Gly Leu Leu Leu Arg Leu Tyr Thr Gln Asn Ile Asp Gly
 80 85 90
 Leu Glu Arg Val Ser Gly Ile Pro Ala Ser Lys Leu Val Glu Ala
 95 100 105
 His Gly Thr Phe Ala Ser Ala Thr Cys Thr Val Cys Gln Arg Pro
 110 115 120
 Phe Pro Gly Glu Asp Ile Arg Ala Asp Val Met Ala Asp Arg Val
 125 130 135
 Pro Arg Cys Pro Val Cys Thr Gly Val Val Lys Pro Asp Ile Val
 140 145 150
 Phe Phe Gly Glu Pro Leu Pro Gln Arg Phe Leu Leu His Val Val
 155 160 165
 Asp Phe Pro Met Ala Asp Leu Leu Leu Ile Leu Gly Thr Ser Leu
 170 175 180
 Glu Val Glu Pro Phe Ala Ser Leu Thr Glu Ala Val Arg Thr Gln
 185 190 195
 Phe Pro Asp Cys Ser Ser Thr Gly Thr Trp Trp Gly Pro Trp Leu
 200 205 210
 Gly Ile Leu Ala Ala Gly Thr Trp Pro Ser Trp Gly Thr Trp Phe
 215 220 225
 Thr Ala Trp Lys Ala
 230

<210> 10
 <211> 446
 <212> PRT
 <213> Homo sapiens

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<220>

<221> misc-feature

<223> Incyte ID No.: 997067CD1

<400> 10

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Met Glu Thr Gln Ala Asp Leu Val Ser Gln Glu Pro Gln Ala Leu
1      5      10      15
Leu Asp Ser Ala Leu Pro Ser Lys Val Pro Ala Phe Ser Asp Lys
20     25     30
Asp Ser Leu Gly Asp Glu Met Leu Ala Ala Ala Leu Leu Lys Ala
35     40     45
Lys Ser Gln Glu Leu Val Thr Phe Glu Asp Val Ala Val Tyr Phe
50     55     60
Ile Arg Lys Glu Trp Lys Arg Leu Glu Pro Ala Gln Arg Asp Leu
65     70     75
Tyr Arg Asp Val Met Leu Glu Asn Tyr Gly Asn Val Phe Ser Leu
80     85     90
Asp Arg Glu Thr Arg Thr Glu Asn Asp Gln Glu Ile Ser Glu Asp
95     100    105
Thr Arg Ser His Gly Val Leu Leu Gly Arg Phe Gln Lys Asp Ile
110    115    120
Ser Gln Gly Leu Lys Phe Lys Glu Ala Tyr Glu Arg Glu Val Ser
125    130    135
Leu Lys Arg Pro Leu Gly Asn Ser Pro Gly Glu Arg Leu Asn Arg
140    145    150
Lys Met Pro Asp Phe Gly Gln Val Thr Val Glu Glu Lys Leu Thr
155    160    165
Pro Arg Gly Glu Arg Ser Glu Lys Tyr Asn Asp Phe Gly Asn Ser
170    175    180
Phe Thr Val Asn Ser Asn Leu Ile Ser His Gln Arg Leu Pro Val
185    190    195
Gly Asp Arg Pro His Lys Cys Asp Glu Cys Ser Lys Ser Phe Asn
200    205    210
Arg Thr Ser Asp Leu Ile Gln His Gln Arg Ile His Thr Gly Glu
215    220    225
Lys Pro Tyr Glu Cys Asn Glu Cys Gly Lys Ala Phe Ser Gln Ser
230    235    240
Ser His Leu Ile Gln His Gln Arg Ile His Thr Gly Glu Lys Pro
245    250    255
Tyr Glu Cys Ser Asp Cys Gly Lys Thr Phe Ser Cys Ser Ser Ala
260    265    270
Leu Ile Leu His Arg Arg Ile His Thr Gly Glu Lys Pro Tyr Glu
275    280    285
Cys Asn Glu Cys Gly Lys Thr Phe Ser Trp Ser Ser Thr Leu Thr
290    295    300
His His Gln Arg Ile His Thr Gly Glu Lys Pro Tyr Ala Cys Asn
305    310    315
Glu Cys Gly Lys Ala Phe Ser Arg Ser Ser Thr Leu Ile His His
320    325    330
Gln Arg Ile His Thr Gly Glu Lys Pro Tyr Glu Cys Asn Glu Cys
335    340    345
Gly Lys Ala Phe Ser Gln Ser Ser His Leu Tyr Gln His Gln Arg
350    355    360
Ile His Thr Gly Glu Lys Pro Tyr Glu Cys Met Glu Cys Gly Gly
365    370    375
Lys Phe Thr Tyr Ser Ser Gly Leu Ile Gln His Gln Arg Ile His
380    385    390
Thr Gly Glu Asn Pro Tyr Glu Cys Ser Glu Cys Gly Lys Ala Phe
395    400    405
Arg Tyr Ser Ser Ala Leu Val Arg His Gln Arg Ile His Thr Gly
410    415    420
Glu Lys Pro Leu Asn Gly Ile Gly Met Ser Lys Ser Ser Leu Arg

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SUBSTITUTE SHEET (RULE 26)

	425	430	435
Val Thr Thr Glu	Leu Asn Ile Arg Glu	Ser Thr	
	440	445	

<210> 11
 <211> 428
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID NO.: 1443262CD1

<400> 11
 Met Glu Pro Leu Lys Val Glu Lys Phe Ala Thr Ala Asn Arg Gly
 1 5 10 15
 Asn Gly Leu Arg Ala Val Thr Pro Leu Arg Pro Gly Glu Leu Leu
 20 25 30
 Phe Arg Ser Asp Pro Leu Ala Tyr Thr Val Cys Lys Gly Ser Arg
 35 40 45
 Gly Val Val Cys Asp Arg Cys Leu Leu Gly Lys Glu Lys Leu Met
 50 55 60
 Arg Cys Ser Gln Cys Arg Val Ala Lys Tyr Cys Ser Ala Lys Cys
 65 70 75
 Gln Lys Lys Ala Trp Pro Asp His Lys Arg Glu Cys Lys Cys Leu
 80 85 90
 Lys Ser Cys Lys Pro Arg Tyr Pro Pro Asp Ser Val Arg Leu Leu
 95 100 105
 Gly Arg Val Val Phe Lys Leu Met Asp Gly Ala Pro Ser Glu Ser
 110 115 120
 Glu Lys Leu Tyr Ser Phe Tyr Asp Leu Glu Ser Asn Ile Asn Lys
 125 130 135
 Leu Thr Glu Asp Lys Lys Glu Gly Leu Arg Gln Leu Val Met Thr
 140 145 150
 Phe Gln His Phe Met Arg Glu Glu Ile Gln Asp Ala Ser Gln Leu
 155 160 165
 Pro Pro Ala Phe Asp Leu Phe Glu Ala Phe Ala Lys Val Ile Cys
 170 175 180
 Asn Ser Phe Thr Ile Cys Asn Ala Glu Met Gln Glu Val Gly Val
 185 190 195
 Gly Leu Tyr Pro Ser Ile Ser Leu Leu Asn His Ser Cys Asp Pro
 200 205 210
 Asn Cys Ser Ile Val Phe Asn Gly Pro His Leu Leu Leu Arg Ala
 215 220 225
 Val Arg Asp Ile Glu Val Gly Glu Glu Leu Thr Ile Cys Tyr Leu
 230 235 240
 Asp Met Leu Met Thr Ser Glu Glu Arg Arg Lys Gln Leu Arg Asp
 245 250 255
 Gln Tyr Cys Phe Glu Cys Asp Cys Phe Arg Cys Gln Thr Gln Asp
 260 265 270
 Lys Asp Ala Asp Met Leu Thr Gly Asp Glu Gln Val Trp Lys Glu
 275 280 285
 Val Gln Glu Ser Leu Lys Lys Ile Glu Glu Leu Lys Ala His Trp
 290 295 300
 Lys Trp Glu Gln Val Leu Ala Met Cys Gln Ala Ile Ile Ser Ser
 305 310 315
 Asn Ser Glu Arg Leu Pro Asp Ile Asn Ile Tyr Gln Leu Lys Val
 320 325 330

Leu Asp Cys Ala Met Asp Ala Cys Ile Asn Leu Gly Leu Leu Glu
 335 340 345
 Glu Ala Leu Phe Tyr Gly Thr Arg Thr Met Glu Pro Tyr Arg Ile
 350 355 360
 Phe Phe Pro Gly Ser His Pro Val Arg Gly Val Gln Val Met Lys
 365 370 375
 Val Gly Lys Leu Gln Leu His Gln Gly Met Phe Pro Gln Ala Met
 380 385 390
 Lys Asn Leu Arg Leu Ala Phe Asp Ile Met Arg Val Thr His Gly
 395 400 405
 Arg Glu His Ser Leu Ile Glu Asp Leu Ile Leu Leu Leu Glu Glu
 410 415 420
 Cys Asp Ala Asn Ile Arg Ala Ser
 425

<210> 12
 <211> 590
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 1521648CD1

<400> 12
 Met Ala Glu Asp Trp Leu Asp Cys Pro Ala Leu Gly Pro Gly Trp
 1 5 10 15
 Lys Arg Arg Glu Val Phe Arg Lys Ser Gly Ala Thr Cys Gly Arg
 20 25 30
 Ser Asp Thr Tyr Trp Gln Ser Pro Thr Gly Asp Arg Ile Arg Ser
 35 40 45
 Lys Val Glu Leu Thr Arg Tyr Leu Gly Pro Ala Cys Asp Leu Thr
 50 55 60
 Leu Phe Asp Phe Lys Gln Gly Ile Leu Cys Tyr Pro Ala Pro Lys
 65 70 75
 Ala His Pro Val Ala Val Ala Ser Lys Lys Arg Lys Lys Pro Ser
 80 85 90
 Arg Pro Ala Lys Thr Arg Lys Arg Gln Val Gly Pro Gln Ser Gly
 95 100 105
 Glu Val Arg Lys Glu Ala Pro Arg Asp Glu Thr Lys Ala Asp Thr
 110 115 120
 Asp Thr Ala Pro Ala Ser Phe Pro Ala Pro Gly Cys Cys Glu Asn
 125 130 135
 Cys Gly Ile Ser Phe Ser Gly Asp Gly Thr Gln Arg Gln Arg Leu
 140 145 150
 Lys Thr Leu Cys Lys Asp Cys Arg Ala Gln Arg Ile Ala Phe Asn
 155 160 165
 Arg Glu Gln Arg Met Phe Lys Arg Val Gly Cys Gly Glu Cys Ala
 170 175 180
 Ala Cys Gln Val Thr Glu Asp Cys Gly Ala Cys Ser Thr Cys Leu
 185 190 195
 Leu Gln Leu Pro His Asp Val Ala Ser Gly Leu Phe Cys Lys Cys
 200 205 210
 Glu Arg Arg Arg Cys Leu Arg Ile Val Glu Arg Ser Arg Gly Cys
 215 220 225
 Gly Val Cys Arg Gly Cys Gln Thr Gln Glu Asp Cys Gly His Cys
 230 235 240
 Pro Ile Cys Leu Arg Pro Pro Arg Pro Gly Leu Arg Arg Gln Trp
 245 250 255

Lys Cys Val Gln Arg Arg Cys Leu Arg Gly Lys His Ala Arg Arg	260	265	270
Lys Gly Gly Cys Asp Ser Lys Met Ala Ala Arg Arg Arg Pro Gly	275	280	285
Ala Gln Pro Leu Pro Pro Pro Pro Ser Gln Ser Pro Glu Pro	290	295	300
Thr Glu Pro His Pro Arg Ala Leu Ala Pro Ser Pro Pro Ala Glu	305	310	315
Phe Ile Tyr Tyr Cys Val Asp Glu Asp Glu Leu Gln Pro Tyr Thr	320	325	330
Asn Arg Arg Gln Asn Arg Lys Cys Gly Ala Cys Ala Ala Cys Leu	335	340	345
Arg Arg Met Asp Cys Gly Arg Cys Asp Phe Cys Cys Asp Lys Pro	350	355	360
Lys Phe Gly Gly Ser Asn Gln Lys Arg Gln Lys Cys Arg Trp Arg	365	370	375
Gln Cys Leu Gln Phe Ala Met Lys Arg Leu Leu Pro Ser Val Trp	380	385	390
Ser Glu Ser Glu Asp Gly Ala Gly Ser Pro Pro Pro Tyr Arg Arg	395	400	405
Arg Lys Arg Pro Ser Ser Ala Arg Arg His His Leu Gly Pro Thr	410	415	420
Leu Lys Pro Thr Leu Ala Thr Arg Thr Ala Gln Pro Asp His Thr	425	430	435
Gln Ala Pro Thr Lys Gln Glu Ala Gly Gly Gly Phe Val Leu Pro	440	445	450
Pro Pro Gly Thr Asp Leu Val Phe Leu Arg Glu Gly Ala Ser Ser	455	460	465
Pro Val Gln Val Pro Gly Pro Val Ala Ala Ser Thr Glu Ala Leu	470	475	480
Leu Gln Val Lys Gln Glu Lys Ala Asp Thr Gln Asp Glu Trp Thr	485	490	495
Pro Gly Thr Ala Val Leu Thr Ser Pro Val Leu Val Pro Gly Cys	500	505	510
Pro Ser Lys Ala Val Asp Pro Gly Leu Pro Ser Val Lys Gln Glu	515	520	525
Pro Pro Asp Pro Glu Glu Asp Lys Glu Asn Lys Asp Asp Ser	530	535	540
Ala Ser Lys Leu Ala Pro Glu Glu Glu Ala Gly Gly Ala Gly Thr	545	550	555
Pro Val Ile Thr Glu Ile Phe Ser Leu Gly Gly Thr Arg Phe Arg	560	565	570
Asp Thr Ala Val Trp Leu Pro Arg Ser Lys Asp Leu Lys Lys Pro	575	580	585
Gly Ala Arg Lys Gln	590		

<210> 13
 <211> 479
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 1685494CD1

<400> 13
 Met Ala Thr Ala Leu Val Ser Ala His Ser Leu Ala Pro Leu Ser

1	5	10	15
Leu Lys Lys Glu Gly	Leu Arg Val Val	Arg Glu Asp His Tyr Ser	
20	25	30	
Thr Trp Glu Gln Gly	Phe Lys Leu Gln Gly	Asn Ser Lys Gly Leu	
35	40	45	
Gly Gln Glu Pro Leu	Cys Lys Gln Phe Arg	Gln Leu Arg Tyr Glu	
50	55	60	
Glu Thr Thr Gly Pro	Arg Glu Ala Leu Ser	Arg Leu Arg Glu Leu	
65	70	75	
Cys Gln Gln Trp Leu	Gln Pro Glu Thr His	Thr Lys Glu Gln Ile	
80	85	90	
Leu Glu Leu Leu Val	Leu Glu Gln Phe Leu	Ile Ile Leu Pro Lys	
95	100	105	
Glu Leu Gln Ala Arg	Val Gln Glu His His	Pro Glu Ser Arg Glu	
110	115	120	
Asp Val Val Val Val	Leu Glu Asp Leu Gln	Leu Asp Leu Gly Glu	
125	130	135	
Thr Gly Gln Gln Val	Asp Pro Asp Gln Pro	Lys Lys Gln Lys Ile	
140	145	150	
Leu Val Glu Glu Met	Ala Pro Leu Lys Gly	Val Gln Glu Gln Gln	
155	160	165	
Val Arg His Glu Cys	Glu Val Thr Lys Pro	Glu Lys Glu Lys Gly	
170	175	180	
Glu Glu Thr Arg Ile	Glu Asn Gly Lys Leu	Ile Val Val Thr Asp	
185	190	195	
Ser Cys Gly Arg Val	Glu Ser Ser Gly Lys	Ile Ser Glu Pro Met	
200	205	210	
Glu Ala His Asn Glu	Gly Ser Asn Leu Glu	Arg His Gln Ala Lys	
215	220	225	
Pro Lys Glu Lys Ile	Glu Tyr Lys Cys Ser	Glu Arg Glu Gln Arg	
230	235	240	
Phe Ile Gln His Leu	Asp Leu Ile Glu His	Ala Ser Thr His Thr	
245	250	255	
Gly Lys Lys Leu Cys	Glu Ser Asp Val Cys	Gln Ser Ser Ser Leu	
260	265	270	
Thr Gly His Lys Lys	Val Leu Ser Arg Glu	Lys Gly His Gln Cys	
275	280	285	
His Glu Cys Gly Lys	Ala Phe Gln Arg Ser	Ser His Leu Val Arg	
290	295	300	
His Gln Lys Ile His	Leu Gly Glu Lys Pro	Tyr Gln Cys Asn Glu	
305	310	315	
Cys Gly Lys Val Phe	Ser Gln Asn Ala Gly	Leu Leu Glu His Leu	
320	325	330	
Arg Ile His Thr Gly	Glu Lys Pro Tyr Leu	Cys Ile His Cys Gly	
335	340	345	
Lys Asn Phe Arg Arg	Ser Ser His Leu Asn	Arg His Gln Arg Ile	
350	355	360	
His Ser Gln Glu Glu	Pro Cys Glu Cys Lys	Glu Cys Gly Lys Thr	
365	370	375	
Phe Ser Gln Ala Leu	Leu Leu Thr His His	Gln Arg Ile His Ser	
380	385	390	
His Ser Lys Ser His	Gln Cys Asn Glu Cys	Gly Lys Ala Phe Ser	
395	400	405	
Leu Thr Ser Asp Leu	Ile Arg His His Arg	Ile His Thr Gly Glu	
410	415	420	
Lys Pro Phe Lys Cys	Asn Ile Cys Gln Lys	Ala Phe Arg Leu Asn	
425	430	435	
Ser His Leu Ala Gln	His Val Arg Ile His	Asn Glu Glu Lys Pro	
440	445	450	
Tyr Gln Cys Ser Glu	Cys Gly Glu Ala Phe	Arg Gln Arg Ser Gly	
455	460	465	
Leu Phe Gln His Gln	Arg Tyr His His Lys	Asp Lys Leu Ala	

470

475

<210> 14
 <211> 433
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 1730829CD1

<400> 14
 Met Glu Ala Val Tyr Leu Val Val Asn Gly Leu Gly Leu Val Leu
 1 5 10 15
 Asp Val Leu Thr Leu Val Leu Asp Leu Asn Phe Leu Leu Val Ser
 20 25 30
 Ser Leu Leu Ala Ser Leu Ala Trp Leu Leu Ala Phe Val Tyr Asn
 35 40 45
 Leu Pro His Thr Val Leu Thr Ser Leu Leu His Leu Gly Arg Gly
 50 55 60
 Val Leu Leu Ser Leu Leu Ala Leu Ile Glu Ala Val Val Arg Phe
 65 70 75
 Thr Cys Gly Gly Leu Gln Ala Leu Cys Thr Leu Leu Tyr Ser Cys
 80 85 90
 Cys Ser Gly Leu Glu Ser Leu Lys Leu Leu Gly His Leu Ala Ser
 95 100 105
 His Gly Ala Leu Arg Ser Arg Glu Ile Leu His Arg Gly Val Leu
 110 115 120
 Asn Val Val Ser Ser Gly His Ala Leu Leu Arg Gln Ala Cys Asp
 125 130 135
 Ile Cys Ala Ile Ala Met Ser Leu Val Ala Tyr Val Ile Asn Ser
 140 145 150
 Leu Val Asn Ile Cys Leu Ile Gly Thr Gln Asn Leu Phe Ser Leu
 155 160 165
 Val Leu Ala Leu Trp Asp Ala Val Thr Gly Pro Leu Trp Arg Met
 170 175 180
 Thr Asp Val Val Ala Ala Phe Leu Ala His Ile Ser Ser Ser Ala
 185 190 195
 Val Ala Met Ala Ile Leu Leu Trp Thr Pro Cys Gln Leu Ala Leu
 200 205 210
 Glu Leu Leu Ala Ser Ala Ala Arg Leu Leu Ala Ser Phe Val Leu
 215 220 225
 Val Asn Leu Thr Gly Leu Val Leu Leu Ala Cys Val Leu Ala Val
 230 235 240
 Thr Val Thr Val Leu His Pro Asp Phe Thr Leu Arg Leu Ala Thr
 245 250 255
 Gln Ala Leu Ser Gln Leu His Ala Arg Pro Ser Tyr His Arg Leu
 260 265 270
 Arg Glu Asp Val Met Arg Leu Ser Arg Leu Ala Leu Gly Ser Glu
 275 280 285
 Ala Trp Arg Arg Val Trp Ser Arg Ser Leu Gln Leu Ala Ser Trp
 290 295 300
 Pro Asn Arg Gly Gly Ala Pro Gly Ala Pro Gln Gly Asp Pro Met
 305 310 315
 Arg Val Phe Ser Val Arg Thr Arg Arg Gln Asp Thr Leu Pro Glu
 320 325 330
 Ala Gly Arg Arg Ser Glu Ala Glu Glu Glu Glu Ala Arg Thr Ile
 335 340 345
 Arg Val Thr Pro Val Arg Gly Arg Glu Arg Leu Asn Glu Glu Glu

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Pro	Pro	Gly	Gly	350	Gln	Asp	Pro	Trp	Lys	355	Leu	Leu	Lys	Glu	Gln	360
				365	Cys	Val	Ile	Cys	Gln	370	Asp	Gln	Ser	Lys	Thr	375
Glu	Arg	Lys	Lys	380	Cys	Arg	His	Leu	Cys	385	Leu	Cys	Gln	Ala	Cys	390
Leu	Leu	Leu	Pro	395	Arg	His	Pro	Val	Tyr	400	His	Arg	Asn	Cys	Pro	405
Glu	Ile	Leu	Met	410	Ile	Leu	Gln	Thr	Leu	415	Asn	Val	Tyr	Leu		420
Cys	Arg	Arg	Gly	425						430						

<210> 15
 <211> 320
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc feature
 <223> Incyte ID No.: 1864641CD1

<400> 15

Met	Pro	Lys	Lys	Lys	Thr	Gly	Ala	Arg	Lys	Lys	Ala	Glu	Asn	Arg		
1				5					10					15		
Arg	Glu	Arg	Glu	Lys	Gln	Leu	Arg	Ala	Ser	Arg	Ser	Thr	Ile	Asp		
				20					25					30		
Leu	Ala	Lys	His	Pro	Cys	Asn	Ala	Ser	Met	Glu	Cys	Asp	Lys	Cys		
				35					40					45		
Gln	Arg	Arg	Gln	Lys	Asn	Arg	Ala	Phe	Cys	Tyr	Phe	Cys	Asn	Ser		
				50					55					60		
Val	Gln	Lys	Leu	Pro	Ile	Cys	Ala	Gln	Cys	Gly	Lys	Thr	Lys	Cys		
				65					70					75		
Met	Met	Lys	Ser	Ser	Asp	Cys	Val	Ile	Lys	His	Ala	Gly	Val	Tyr		
				80					85					90		
Ser	Thr	Gly	Leu	Ala	Met	Val	Gly	Ala	Ile	Cys	Asp	Phe	Cys	Glu		
				95					100					105		
Ala	Trp	Val	Cys	His	Gly	Arg	Lys	Cys	Leu	Ser	Thr	His	Ala	Cys		
				110					115					120		
Ala	Cys	Pro	Leu	Thr	Asp	Ala	Glu	Cys	Val	Glu	Cys	Glu	Arg	Gly		
				125					130					135		
Val	Trp	Asp	His	Gly	Gly	Arg	Ile	Phe	Ser	Cys	Ser	Phe	Cys	His		
				140					145					150		
Asn	Phe	Leu	Cys	Glu	Asp	Asp	Gln	Phe	Glu	His	Gln	Ala	Ser	Cys		
				155					160					165		
Gln	Val	Leu	Glu	Ala	Glu	Thr	Phe	Lys	Cys	Val	Ser	Cys	Asn	Arg		
				170					175					180		
Leu	Gly	Gln	His	Ser	Cys	Leu	Arg	Cys	Lys	Ala	Cys	Phe	Cys	Asp		
				185					190					195		
Asp	His	Thr	Arg	Ser	Lys	Val	Phe	Lys	Gln	Glu	Lys	Gly	Lys	Gln		
				200					205					210		
Pro	Pro	Cys	Pro	Lys	Cys	Gly	His	Glu	Thr	Gln	Glu	Thr	Lys	Asp		
				215					220					225		
Leu	Ser	Met	Ser	Thr	Arg	Ser	Leu	Lys	Phe	Gly	Arg	Gln	Thr	Gly		
				230					235					240		
Gly	Glu	Glu	Gly	Asp	Gly	Ala	Ser	Gly	Tyr	Asp	Ala	Tyr	Trp	Lys		
				245					250					255		
Asn	Leu	Ser	Ser	Asp	Lys	Tyr	Gly	Asp	Thr	Ser	Tyr	His	Asp	Glu		
				260					265					270		
Glu	Glu	Asp	Glu	Tyr	Glu	Ala	Glu	Asp	Asp	Glu	Glu	Glu	Glu	Asp		

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	275		280		285
Glu Gly Arg Lys	Asp Ser Asp Thr Glu Ser Ser Asp Leu Phe Thr				
	290		295		300
Asn Leu Asn Leu	Gly Arg Thr Tyr Ala Ser Gly Tyr Ala His Tyr				
	305		310		315
Glu Glu Gln Glu	Asn				
	320				

<210> 16
 <211> 179
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 2444604CD1

<400> 16
 Met Ala Ala Gly Phe Phe Gln Pro Phe Met Ser Pro Arg Phe Pro
 1 5 10 15
 Gly Gly Pro Arg Pro Thr Leu Arg Met Pro Ser Gln Pro Pro Ala
 20 25 30
 Cys Leu Pro Gly Ser Gln Pro Leu Leu Pro Gly Ala Met Glu Pro
 35 40 45
 Ser Pro Arg Ala Gln Gly His Pro Ser Met Gly Gly Pro Met Gln
 50 55 60
 Arg Val Thr Pro Pro Arg Gly Met Ala Ser Val Gly Pro Gln Ser
 65 70 75
 Tyr Gly Gly Gly Met Arg Pro Pro Pro Asn Ser Leu Ala Gly Pro
 80 85 90
 Gly Leu Pro Ala Met Asn Met Gly Pro Gly Val Arg Gly Pro Trp
 95 100 105
 Ala Ser Pro Ser Gly Asn Ser Ile Pro Tyr Ser Ser Ser Ser Pro
 110 115 120
 Gly Ser Tyr Thr Gly Pro Pro Gly Gly Gly Gly Pro Pro Gly Thr
 125 130 135
 Pro Ile Met Pro Ser Pro Gly Asp Ser Thr Asn Ser Ser Glu Asn
 140 145 150
 Met Tyr Thr Ile Met Asn Pro Ile Gly Gln Gly Ala Gly Arg Ala
 155 160 165
 Asn Phe Pro Leu Gly Pro Gly Pro Glu Gly Pro Trp Pro Pro
 170 175

<210> 17
 <211> 494
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 2445008CD1

<400> 17
 Met Gly Arg Lys Lys Lys Lys Gln Leu Lys Pro Trp Cys Trp Tyr
 1 5 10 15
 Cys Asn Arg Asp Phe Asp Asp Glu Lys Ile Leu Ile Gln His Gln

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SUBSTITUTE SHEET (RULE 26)

	20		25		30
Lys Ala Lys His Phe	Lys Cys His Ile Cys	His Lys Lys Leu Tyr			
35	40	45			
Thr Gly Pro Gly Leu	Ala Ile His Cys Met	Gln Val His Lys Glu			
50	55	60			
Thr Ile Asp Ala Val	Pro Asn Ala Ile Pro	Gly Arg Thr Asp Ile			
65	70	75			
Glu Leu Glu Ile Tyr	Gly Met Glu Gly Ile	Pro Glu Lys Asp Met			
80	85	90			
Asp Glu Arg Arg Arg	Leu Leu Glu Gln Lys	Thr Gln Glu Ser Gln			
95	100	105			
Lys Lys Lys Gln Gln	Asp Asp Ser Asp Glu	Tyr Asp Asp Asp Asp			
110	115	120			
Ser Ala Ala Ser Thr	Ser Phe Gln Pro Gln	Pro Val Gln Pro Gln			
125	130	135			
Gln Gly Tyr Ile Pro	Pro Met Ala Gln Pro	Gly Leu Pro Pro Val			
140	145	150			
Pro Gly Ala Pro Gly	Met Pro Pro Gly Ile	Pro Pro Leu Met Pro			
155	160	165			
Gly Val Pro Pro Leu	Met Pro Gly Met Pro	Pro Val Met Pro Gly			
170	175	180			
Met Pro Pro Gly Leu	His His Gln Arg Lys	Tyr Thr Gln Ser Phe			
185	190	195			
Cys Gly Glu Asn Ile	Met Met Pro Met Gly	Gly Met Met Pro Pro			
200	205	210			
Gly Pro Gly Ile Pro	Pro Pro Leu Met Pro	Gly Met Pro Pro Gly			
215	220	225			
Pro Pro Pro Val Pro	Arg Pro Gly Ile Pro	Pro Met Thr Gln Ala			
230	235	240			
Gln Ala Val Ser Ala	Pro Gly Ile Leu Asn	Arg Pro Pro Ala Pro			
245	250	255			
Thr Ala Thr Val Pro	Ala Pro Gln Pro Pro	Val Thr Lys Pro Leu			
260	265	270			
Phe Pro Ser Ala Gly	Gln Met Gly Thr Pro	Val Thr Ser Ser Ser			
275	280	285			
Thr Ala Ser Ser Asn	Ser Glu Ser Leu Ser	Ala Ser Ser Lys Ala			
290	295	300			
Leu Phe Pro Ser Thr	Ala Gln Ala Gln Ala	Ala Val Gln Gly Pro			
305	310	315			
Val Gly Thr Asp Phe	Lys Pro Leu Asn Ser	Thr Pro Ala Thr Thr			
320	325	330			
Thr Glu Pro Pro Lys	Pro Thr Phe Pro Ala	Tyr Thr Gln Ser Thr			
335	340	345			
Ala Ser Thr Thr Ser	Thr Thr Asn Ser Thr	Ala Ala Lys Pro Ala			
350	355	360			
Ala Ser Ile Thr Ser	Lys Pro Ala Thr Leu	Thr Thr Thr Ser Ala			
365	370	375			
Thr Ser Lys Leu Ile	His Pro Asp Glu Asp	Ile Ser Leu Glu Glu			
380	385	390			
Arg Arg Ala Gln Leu	Pro Lys Tyr Gln Arg	Asn Leu Pro Arg Pro			
395	400	405			
Gly Gln Ala Pro Ile	Gly Asn Pro Pro Val	Gly Pro Ile Gly Gly			
410	415	420			
Met Met Pro Pro Gln	Pro Gly Ile Pro Gln	Gln Gln Gly Met Arg			
425	430	435			
Pro Pro Met Pro Pro	His Gly Gln Tyr Gly	Gly His His Gln Gly			
440	445	450			
Met Pro Gly Tyr Leu	Pro Gly Ala Met Pro	Pro Tyr Gly Gln Gly			
455	460	465			
Pro Pro Met Val Pro	Pro Tyr Gln Gly Gly	Pro Pro Arg Pro Pro			
470	475	480			

Met Gly Met Arg Pro Pro Val Met Ser Gln Gly Gly Arg Tyr
485 490

<210> 18
<211> 401
<212> PRT
<213> Homo sapiens

<220>
<221> misc-feature
<223> Incyte ID No.: 2572462CD1

<400> 18
Met Ala Ser Ser Pro Arg Pro Lys Met Asp Ala Ile Leu Thr Glu
1 5 10 15
Ala Ile Lys Ala Cys Phe Gln Lys Ser Gly Ala Ser Val Val Ala
20 25 30
Ile Arg Lys Tyr Ile Ile His Lys Tyr Pro Ser Leu Glu Leu Glu
35 40 45
Arg Arg Gly Tyr Leu Leu Lys Gln Ala Leu Lys Arg Glu Leu Asn
50 55 60
Arg Gly Val Ile Lys Gln Val Lys Gly Lys Gly Ala Ser Gly Ser
65 70 75
Phe Val Val Val Gln Lys Ser Arg Lys Thr Pro Gln Lys Ser Arg
80 85 90
Asn Arg Lys Asn Arg Ser Ser Ala Val Asp Pro Glu Pro Gln Val
95 100 105
Lys Leu Glu Asp Val Leu Pro Leu Ala Phe Thr Arg Leu Cys Glu
110 115 120
Pro Lys Glu Ala Ser Tyr Ser Leu Ile Arg Lys Tyr Val Ser Gln
125 130 135
Tyr Tyr Pro Lys Leu Arg Val Asp Ile Arg Pro Gln Leu Leu Lys
140 145 150
Asn Ala Leu Gln Arg Ala Val Glu Arg Gly Gln Leu Glu Gln Ile
155 160 165
Thr Gly Lys Gly Ala Ser Gly Thr Phe Gln Leu Lys Lys Ser Gly
170 175 180
Glu Lys Pro Leu Leu Gly Gly Ser Leu Met Glu Tyr Ala Ile Leu
185 190 195
Ser Ala Ile Ala Ala Met Asn Glu Pro Lys Thr Cys Ser Thr Thr
200 205 210
Ala Leu Lys Lys Tyr Val Leu Glu Asn His Pro Gly Thr Asn Ser
215 220 225
Asn Tyr Gln Met His Leu Leu Lys Lys Thr Leu Gln Lys Cys Glu
230 235 240
Lys Asn Gly Trp Met Glu Gln Ile Ser Gly Lys Gly Phe Ser Gly
245 250 255
Thr Phe Gln Leu Cys Phe Pro Tyr Tyr Pro Ser Pro Gly Val Leu
260 265 270
Phe Pro Lys Lys Glu Pro Asp Asp Ser Arg Asp Glu Asp Glu Asp
275 280 285
Glu Asp Glu Ser Ser Glu Glu Asp Ser Glu Asp Glu Glu Pro Pro
290 295 300
Pro Lys Arg Arg Leu Gln Lys Lys Thr Pro Ala Lys Ser Pro Gly
305 310 315
Lys Ala Ala Ser Val Lys Gln Arg Gly Ser Lys Pro Ala Pro Lys
320 325 330
Val Ser Ala Ala Gln Arg Gly Lys Ala Arg Pro Leu Pro Lys Lys
335 340 345

Ala Pro Pro Lys	Ala Lys Thr Pro Ala	Lys Lys Thr Arg Pro Ser	
	350	355	360
Ser Thr Val Ile	Lys Lys Pro Ser Gly	Gly Ser Ser Lys Lys Pro	
	365	370	375
Ala Thr Ser Ala	Arg Lys Glu Val Lys	Leu Pro Gly Lys Gly Lys	
	380	385	390
Ser Thr Met Lys	Lys Ser Phe Arg Val	Lys Lys	
	395	400	

<210> 19
 <211> 264
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 2572892CD1

<400> 19

Met Pro Arg Ser Phe Leu Val Arg Lys Pro Ser Asp Pro Asn Arg	
1 5 10 15	
Lys Pro Asn Tyr Ser Glu Leu Gln Asp Ser Asn Pro Glu Phe Thr	
20 25 30	
Phe Gln Gln Pro Tyr Asp Gln Ala His Leu Leu Ala Ala Ile Pro	
35 40 45	
Pro Pro Glu Ile Leu Asn Pro Thr Ala Ser Leu Pro Met Leu Ile	
50 55 60	
Trp Asp Ser Val Leu Ala Pro Gln Ala Gln Pro Ile Ala Trp Ala	
65 70 75	
Ser Leu Arg Leu Gln Glu Ser Pro Arg Val Ala Glu Leu Thr Ser	
80 85 90	
Leu Ser Asp Glu Asp Ser Gly Lys Gly Ser Gln Pro Pro Ser Pro	
95 100 105	
Pro Ser Pro Ala Pro Ser Ser Phe Ser Ser Thr Ser Ala Ser Ser	
110 115 120	
Leu Glu Ala Glu Ala Tyr Ala Ala Phe Pro Gly Leu Gly Gln Val	
125 130 135	
Pro Lys Gln Leu Ala Gln Leu Ser Glu Ala Lys Asp Leu Gln Ala	
140 145 150	
Arg Lys Ala Phe Asn Cys Lys Tyr Cys Asn Lys Glu Tyr Leu Ser	
155 160 165	
Leu Gly Ala Leu Lys Met His Ile Arg Ser His Thr Leu Pro Cys	
170 175 180	
Val Cys Gly Thr Cys Gly Lys Ala Phe Ser Arg Pro Trp Leu Leu	
185 190 195	
Gln Gly His Val Arg Thr His Thr Gly Glu Lys Pro Phe Ser Cys	
200 205 210	
Pro His Cys Ser Arg Ala Phe Ala Asp Arg Ser Asn Leu Arg Ala	
215 220 225	
His Leu Gln Thr His Ser Asp Val Lys Lys Tyr Gln Cys Gln Ala	
230 235 240	
Cys Ala Arg Thr Phe Ser Arg Met Ser Leu Leu His Lys His Gln	
245 250 255	
Glu Ser Gly Cys Ser Gly Cys Pro Arg	
260	

<210> 20
 <211> 153
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 2785674CD1

<400> 20
 Met Thr Lys Ile Lys Ala Asp Pro Asp Gly Pro Glu Ala Gln Ala
 1 5 10 15
 Glu Ala Cys Ser Gly Glu Arg Thr Tyr Gln Glu Leu Leu Val Asn
 20 25 30
 Gln Asn Pro Ile Ala Gln Pro Leu Ala Ser Arg Arg Leu Thr Arg
 35 40 45
 Lys Leu Tyr Lys Cys Ile Lys Lys Ala Val Lys Gln Lys Gln Ile
 50 55 60
 Arg Arg Gly Val Lys Glu Val Gln Lys Phe Val Asn Lys Gly Glu
 65 70 75
 Lys Gly Ile Met Val Leu Ala Gly Asp Thr Leu Pro Ile Glu Val
 80 85 90
 Tyr Cys His Leu Pro Val Met Cys Glu Asp Arg Asn Leu Pro Tyr
 95 100 105
 Val Tyr Ile Pro Ser Lys Thr Asp Leu Gly Ala Ala Ala Gly Ser
 110 115 120
 Lys Arg Pro Thr Cys Val Ile Met Val Lys Pro His Glu Glu Tyr
 125 130 135
 Gln Glu Ala Tyr Asp Glu Cys Leu Glu Glu Val Gln Ser Leu Pro
 140 145 150
 Leu Pro Leu

<210> 21
 <211> 243
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 2797479CD1

<400> 21
 Met Gly Asp Asp Ile Ser Thr His Ile Ala Pro Lys Glu Leu Arg
 1 5 10 15
 His Lys His Pro Ser Ser Val Asp Glu Val Ala Gln Val Val Lys
 20 25 30
 Gln Leu Arg Ile Ile Leu Gln Gln Gln Val Arg Pro Gly Glu Ser
 35 40 45
 Thr Val Leu Ala Leu Arg Pro Asn Val Gln Gln Ile Glu Ala Pro
 50 55 60
 Asp Val Ser Arg Asp Pro Arg Val Leu Gly Phe Asp Phe Pro Gly
 65 70 75
 Ser Ala Arg Ile His Glu Gly Thr His Thr Leu Glu Lys Pro Tyr
 80 85 90
 Glu Cys Lys Gln Cys Gly Lys Leu Leu Ser His Arg Ser Ser Phe
 95 100 105
 Arg Arg His Met Met Ala His Thr Gly Asp Gly Pro His Lys Cys
 110 115 120
 Thr Val Cys Gly Lys Ala Phe Asp Ser Pro Ser Val Phe Gln Arg

His Glu Arg Thr	125	130	135
His Thr Gly Glu Lys	140	Pro Tyr Glu Cys Lys	Gln
Cys Gly Lys Ala	145	150	
Phe Arg Thr Ser Ser	155	Ser Leu Arg Lys His	Glu
Thr Thr His Thr	160	165	
Gly Glu-Gln Pro Tyr	170	Lys Cys Lys Cys Gly	Lys
	175	180	
Ala Phe Ser Asp	185	Leu Phe Ser Phe Gln	Ser His Glu Thr Thr His
Ser Glu Glu Glu	190	195	
Pro Tyr Glu Cys Lys	200	Glu Cys Gly Lys Ala	Phe
Ser Ser Phe Lys	205	210	
Tyr Phe Cys Arg His	215	Glu Arg Thr His Ser	Glu
Glu Lys Ser Tyr	220	225	
Gly Cys Gln Ile Cys	230	Gly Lys Leu Ser Val	Val
Ser Val Thr	235	240	

<210> 22
 <211> 485
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 2960640CD1

<400> 22

Met Arg Asp Asn Arg Ala Val Ser Leu Cys Gln Gln Glu Trp Met	1	5	10	15
Cys Pro Gly Pro Ala Gln Arg Ala Leu Tyr Arg Gly Ala Thr Gln	20	25	30	
Arg Lys Asp Ser His Val Ser Leu Ala Thr Gly Val Pro Trp Gly	35	40	45	
Tyr Glu Glu Thr Lys Thr Leu Leu Ala Ile Leu Ser Ser Ser Gln	50	55	60	
Phe Tyr Gly Lys Leu Gln Thr Cys Gln Gln Asn Ser Gln Ile Tyr	65	70	75	
Arg Ala Met Ala Glu Gly Leu Trp Glu Gln Gly Phe Leu Arg Thr	80	85	90	
Pro Glu Gln Cys Arg Thr Lys Phe Lys Ser Leu Gln Leu Ser Tyr	95	100	105	
Arg Lys Val Arg Arg Gly Arg Val Pro Glu Pro Cys Ile Phe Tyr	110	115	120	
Glu Glu Met Asn Ala Leu Ser Gly Ser Trp Ala Ser Ala Pro Pro	125	130	135	
Met Ala Ser Asp Ala Val Pro Gly Gln Glu Gly Ser Asp Ile Glu	140	145	150	
Ala Gly Glu Leu Asn His Gln Asn Gly Glu Pro Thr Glu Val Glu	155	160	165	
Asp Gly Thr Val Asp Gly Ala Asp Arg Asp Glu Lys Asp Phe Arg	170	175	180	
Asn Pro Gly Gln Glu Val Arg Lys Leu Asp Leu Pro Val Leu Phe	185	190	195	
Pro Asn Arg Leu Gly Phe Glu Phe Lys Asn Glu Ile Lys Lys Glu	200	205	210	
Asn Leu Lys Trp Asp Asp Ser Glu Glu Val Glu Ile Asn Lys Ala	215	220	225	
Leu Gln Arg Lys Ser Arg Gly Val Tyr Trp His Ser Glu Leu Gln				

Lys Gly Leu Glu	230	235	240
Ser Glu Pro Thr Ser Arg Arg Gln Cys Arg Asn	245	250	255
Ser Pro Gly Glu Ser Glu Glu Lys Thr Pro Ser Gln Glu Lys Met	260	265	270
Ser His Gln Ser Phe Cys Ala Arg Asp Lys Ala Cys Thr His Ile	275	280	285
Leu Cys Gly Lys Asn Cys Ser Gln Ser Val His Ser Pro His Lys	290	295	300
Pro Ala Leu Lys Leu Glu Lys Val Ser Gln Cys Pro Glu Cys Gly	305	310	315
Lys Thr Phe Ser Arg Ser Ser Tyr Leu Val Arg His Gln Arg Ile	320	325	330
His Thr Gly Glu Lys Pro His Lys Cys Ser Glu Cys Gly Lys Gly	335	340	345
Phe Ser Glu Arg Ser Asn Leu Thr Ala His Leu Arg Thr His Thr	350	355	360
Gly Glu Arg Pro Tyr Gln Cys Gly Gln Cys Gly Lys Ser Phe Asn	365	370	375
Gln Ser Ser Ser Leu Ile Val His Gln Arg Thr His Thr Gly Glu	380	385	390
Lys Pro Tyr Gln Cys Ile Val Cys Gly Lys Arg Phe Asn Asn Ser	395	400	405
Ser Gln Phe Ser Ala His Arg Arg Ile His Thr Gly Glu Ser Pro	410	415	420
Tyr Lys Cys Ala Val Cys Gly Lys Ile Phe Asn Asn Ser Ser His	425	430	435
Phe Ser Ala His Arg Lys Thr His Thr Gly Glu Lys Pro Tyr Arg	440	445	450
Cys Ser His Cys Glu Arg Gly Phe Thr Lys Asn Ser Ala Leu Thr	455	460	465
Arg His Gln Thr Val His Met Lys Ala Val Leu Ser Ser Gln Glu	470	475	480
Gly Arg Asp Ala Leu	485		

<210> 23

<211> 160

<212> PRT

<213> Homo sapiens

<220>

<221> misc-feature

<223> Incyte ID No.: 3454051CD1

<400> 23

Met Ser Trp Thr Cys Pro Arg Cys Gln Gln Pro Val Phe Phe Ala	
1 5 10 15	
Glu Lys Val Ser Ser Leu Gly Lys Asn Trp His Arg Phe Cys Leu	
20 25 30	
Lys Cys Glu Arg Cys His Ser Ile Leu Ser Pro Gly Gly His Ala	
35 40 45	
Glu His Asn Gly Arg Pro Tyr Cys His Lys Pro Cys Tyr Gly Ala	
50 55 60	
Leu Phe Gly Pro Arg Gly Pro Pro His Met Lys Thr Phe Thr Gly	
65 70 75	
Glu Thr Ser Leu Cys Pro Gly Cys Gly Glu Pro Val Tyr Phe Ala	
80 85 90	

Glu Lys Val Met Ser Leu Gly Arg Asn Trp His Arg Pro Cys Leu
 95 100 105
 Arg Cys Gln Arg Cys His Lys Thr Leu Thr Ala Gly Ser His Ala
 110 115 120
 Glu His Asp Gly Val Pro Tyr Cys His Val Pro Cys Tyr Gly Tyr
 125 130 135
 Leu Phe Gly Pro Lys Gly Val Asn Ile Gly Asp Val Gly Cys Tyr
 140 145 150
 Ile Tyr Asp Pro Val Lys Ile Lys Phe Lys
 155 160

<210> 24
 <211> 511
 <212> PRT
 <213> Homo sapiens

<220>
 <221>
 <223> Incyte ID No.: 3510640CD1

<400> 24
 Met Gln Glu Leu Tyr Ser Thr Pro Ala Ser Arg Leu Asp Ser Phe
 1 5 10 15
 Val Ala Gln Trp Leu Gln Pro His Arg Glu Trp Lys Glu Glu Val
 20 25 30
 Leu Asp Ala Val Arg Thr Val Glu Glu Phe Leu Arg Gln Glu His
 35 40 45
 Phe Gln Gly Lys Arg Gly Leu Asp Gln Asp Val Arg Val Leu Lys
 50 55 60
 Val Val Lys Val Gly Ser Phe Gly Asn Gly Thr Val Leu Arg Ser
 65 70 75
 Thr Arg Glu Val Glu Leu Val Ala Phe Leu Ser Cys Phe His Ser
 80 85 90
 Phe Gln Glu Ala Ala Lys His His Lys Asp Val Leu Arg Leu Ile
 95 100 105
 Trp Lys Thr Met Trp Gln Ser Gln Asp Leu Leu Asp Leu Gly Leu
 110 115 120
 Glu Asp Leu Arg Met Glu Gln Arg Val Pro Asp Ala Leu Val Phe
 125 130 135
 Thr Ile Gln Thr Arg Gly Thr Ala Glu Pro Ile Thr Val Thr Ile
 140 145 150
 Val Pro Ala Tyr Arg Ala Leu Gly Pro Ser Leu Pro Asn Ser Gln
 155 160 165
 Pro Pro Pro Glu Val Tyr Val Ser Leu Ile Lys Ala Cys Gly Gly
 170 175 180
 Pro Gly Asn Phe Cys Pro Phe Phe Ser Glu Leu Gln Arg Asn Phe
 185 190 195
 Val Lys His Arg Pro Thr Lys Leu Lys Ser Leu Leu Arg Leu Val
 200 205 210
 Lys His Trp Tyr Gln Gln Tyr Val Lys Ala Arg Ser Pro Arg Ala
 215 220 225
 Asn Leu Pro Pro Leu Tyr Ala Leu Glu Leu Leu Thr Ile Tyr Ala
 230 235 240
 Trp Glu Met Gly Thr Glu Glu Asp Glu Asn Phe Met Leu Asp Glu
 245 250 255
 Gly Phe Thr Thr Val Met Asp Leu Leu Leu Glu Tyr Glu Val Ile
 260 265 270
 Cys Ile Tyr Trp Thr Lys Tyr Tyr Thr Leu His Asn Ala Ile Ile

	275		280		285
Glu Asp Cys Val	Arg Lys Gln Leu Lys	Lys Glu Arg Pro Ile Ile			
	290		295		300
Leu Asp Pro Ala	Asp Pro Thr Leu Asn	Val Ala Glu Gly Tyr Arg			
	305		310		315
Trp Asp Ile Val	Ala Gln Arg Ala Ser	Gln Cys Leu Lys Gln Asp			
	320		325		330
Cys Cys Tyr Asp	Asn Arg Glu Asn Pro	Ile Ser Ser Trp Asn Val			
	335		340		345
Lys Arg Ala Arg	Asp Ile His Leu Thr	Val Glu Gln Arg Gly Tyr			
	350		355		360
Pro Asp Phe Asn	Leu Ile Val Asn Pro	Tyr Glu Pro Ile Arg Lys			
	365		370		375
Val Lys Glu Lys	Ile Arg Arg Thr Arg	Gly Tyr Ser Gly Leu Gln			
	380		385		390
Arg Leu Ser Phe	Gln Val Pro Gly Ser	Glu Arg Gln Leu Leu Ser			
	395		400		405
Ser Arg Cys Ser	Leu Ala Lys Tyr Gly	Ile Phe Ser His Thr His			
	410		415		420
Ile Tyr Leu Leu	Glu Thr Ile Pro Ser	Glu Ile Gln Val Phe Val			
	425		430		435
Lys Asn Pro Asp	Gly Gly Ser Tyr Ala	Tyr Ala Ile Asn Pro Asn			
	440		445		450
Ser Phe Ile Leu	Gly Leu Lys Gln Gln	Ile Glu Asp Gln Gln Gly			
	455		460		465
Leu Pro Lys Lys	Gln Gln Gln Leu Glu	Phe Gln Gly Gln Val Leu			
	470		475		480
Gln Asp Trp Leu	Gly Leu Gly Ile Tyr	Gly Ile Gln Asp Ser Asp			
	485		490		495
Thr Leu Ile Leu	Ser Lys Lys Lys Gly	Glu Ala Leu Phe Pro Ala			
	500		505		510
Ser					

<210> 25
 <211> 310
 <212> PRT
 <213> Homo sapiens

<220> -
 <223> Incyte ID No.: 3815083CD1

<400> 25

Met Arg Pro Leu Gln Ile Val Pro Ser Arg Leu Ile Ser Gln Leu	
1 5 10 15	
Tyr Cys Gly Leu Lys Pro Pro Ala Ser Thr Arg Asn Gln Ile Cys	
20 25 30	
Leu Lys Met Ala Arg Pro Ser Ser Ser Met Ala Asp Phe Arg Lys	
35 40 45	
Phe Phe Ala Lys Ala Lys His Ile Val Ile Ile Ser Gly Ala Gly	
50 55 60	
Val Ser Ala Glu Ser Gly Val Pro Thr Phe Arg Gly Ala Gly Gly	
65 70 75	
Tyr Trp Arg Lys Trp Gln Ala Gln Asp Leu Ala Thr Pro Leu Ala	
80 85 90	
Phe Ala His Asn Pro Ser Arg Val Trp Glu Phe Tyr His Tyr Arg	
95 100 105	
Arg Glu Val Met Gly Ser Lys Glu Pro Asn Ala Gly His Arg Ala	
110 115 120	

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Ile Ala Glu Cys Glu Thr Arg Leu Gly Lys Gln Gly Arg Arg Val
125 130 135
Val Val Ile Thr Gln Asn Ile Asp Glu Leu His Arg Lys Ala Gly
140 145 150
Thr Lys Asn Leu Leu Glu Ile His Gly Ser Leu Phe Lys Thr Arg
155 160 165
Cys Thr Ser Cys Gly Val Val Ala Glu Asn Tyr Lys Ser Pro Ile
170 175 180
Cys Pro Ala Leu Ser Gly Lys Gly Ala Pro Glu Pro Gly Thr Gln
185 190 195
Asp Ala Ser Ile Pro Val Glu Lys Leu Pro Arg Cys Glu Glu Ala
200 205 210
Gly Cys Gly Gly Leu Leu Arg Pro His Val Val Trp Phe Gly Glu
215 220 225
Asn Leu Asp Pro Ala Ile Leu Glu Glu Val Asp Arg Glu Leu Ala
230 235 240
His Cys Asp Leu Cys Leu Val Val Gly Thr Ser Ser Val Val Tyr
245 250 255
Pro Ala Ala Met Phe Ala Pro Gln Val Ala Ala Arg Gly Val Pro
260 265 270
Val Ala Glu Phe Asn Thr Glu Thr Thr Pro Ala Thr Asn Arg Phe
275 280 285
Arg Phe His Phe Gln Gly Pro Cys Gly Thr Thr Leu Pro Glu Ala
290 295 300
Leu Ala Cys His Glu Asn Glu Thr Val Ser
305 310

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<210> 26
 <211> 331
 <212> PRT
 <213> Homo sapiens

<220> -
 <221> misc-feature
 <223> Incyte ID No.: 3988457CD1

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<400> 26
Met Ala Ile Asn Arg Phe Arg Leu Glu Asn Asp Leu Glu Glu Leu
1 5 10 15
Ala Leu Tyr Gln Ile Gln Leu Leu Lys Asp Leu Arg His Thr Glu
20 25 30
Asn Glu Glu Asp Lys Val Ser Ser Ser Ser Phe Arg Gln Arg Met
35 40 45
Leu Gly Asn Leu Leu Arg Pro Pro Tyr Glu Arg Pro Glu Leu Pro
50 55 60
Thr Cys Leu Tyr Val Ile Gly Leu Thr Gly Ile Ser Gly Ser Gly
65 70 75
Lys Ser Ser Ile Ala Gln Arg Leu Lys Gly Leu Gly Ala Phe Val
80 85 90
Ile Asp Ser Asp His Leu Gly His Arg Ala Tyr Ala Pro Gly Gly
95 100 105
Pro Ala Tyr Gln Pro Val Val Glu Ala Phe Gly Thr Asp Ile Leu
110 115 120
His Lys Asp Gly Ile Ile Asn Arg Lys Val Leu Gly Ser Arg Val
125 130 135
Phe Gly Asn Lys Lys Gln Leu Lys Ile Leu Thr Asp Ile Met Trp
140 145 150
Pro Ile Ile Ala Lys Leu Ala Arg Glu Glu Met Asp Arg Ala Val
155 160 165
Ala Glu Gly Lys Arg Val Cys Val Ile Asp Ala Ala Val Leu Leu
170 175 180

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Glu	Ala	Gly	Trp	Gln	Asn	Leu	Val	His	Glu	Val	Trp	Thr	Ala	Val	185	190	195
Ile	Pro	Glu	Thr	Glu	Ala	Val	Arg	Arg	Ile	Val	Glu	Arg	Asp	Gly	200	205	210
Leu	Ser	Glu	Ala	Ala	Ala	Gln	Ser	Arg	Leu	Gln	Ser	Gln	Met	Ser	215	220	225
Gly	Gln	Gln	Leu	Val	Glu	Gln	Ser	His	Val	Val	Leu	Ser	Ser	Pro	230	235	240
Cys	Gly	Ser	Arg	Ile	Ser	Pro	Asn	Ala	Arg	Trp	Arg	Lys	Pro	Gly	245	250	255
Pro	Ser	Cys	Arg	Ser	Ala	Phe	Pro	Arg	Leu	Ile	Arg	Pro	Ser	Thr	260	265	270
Glu	Lys	Phe	Ser	Val	Gly	Pro	Asp	Trp	Leu	Leu	Glu	Leu	Thr	Ser	275	280	285
Asp	Pro	Val	Val	Arg	Arg	Asn	Gly	Gly	Leu	Asp	Ala	His	Pro	Gly	290	295	300
Ser	Gly	Pro	Glu	Val	Gln	Ala	Ile	Leu	Cys	Arg	Thr	Trp	Pro	Gly	305	310	315
Leu	Val	Asp	Thr	Gly	Ser	Leu	Pro	Asn	Thr	Leu	Val	Phe	Gly	Gln	320	325	330

His

<210> 27
 <211> 200
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> misc-feature
 <223> Incyte ID No.: 131890CD1

<400> 27
 Met Met Thr Ala Glu Ser Arg Glu Ala Thr Gly Leu Ser Pro Gln
 1 5 10 15
 Ala Ala Gln Glu Lys Asp Gly Ile Val Ile Val Lys Val Glu Glu
 20 25 30
 Glu Asp Glu Glu Asp His Met Trp Gly Gln Asp Ser Thr Leu Gln
 35 40 45
 Asp Thr Pro Pro Pro Asp Pro Glu Ile Phe Arg Gln Arg Phe Arg
 50 55 60
 Arg Phe Cys Tyr Gln Asn Thr Phe Gly Pro Arg Glu Ala Leu Ser
 65 70 75
 Arg Leu Lys Glu Leu Cys His Gln Trp Leu Arg Pro Glu Ile Asn
 80 85 90
 Thr Lys Glu Gln Ile Leu Glu Leu Leu Val Leu Glu Gln Phe Leu
 95 100 105
 Ser Ile Leu Pro Lys Glu Leu Gln Val Trp Leu Gln Glu Tyr Arg
 110 115 120
 Pro Asp Ser Gly Glu Glu Ala Val Thr Leu Leu Glu Asp Leu Glu
 125 130 135
 Leu Asp Leu Ser Gly Gln Gln Val Pro Gly Gln Val His Gly Pro
 140 145 150
 Glu Met Leu Ala Arg Gly Met Val Pro Leu Asp Pro Val Gln Glu
 155 160 165
 Ser Ser Ser Phe Asp Leu His His Glu Ala Thr Gln Ser His Phe
 170 175 180
 Lys His Ser Ser Arg Lys Pro Arg Leu Leu Gln Ser Arg Gly Lys
 185 190 195
 Lys Gln Gly Phe Ile

200

<210> 28
 <211> 100
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 238642CD1

<400> 28
 Met Gln Lys Pro Cys Lys Glu Asn Glu Gly Lys Pro Lys Cys Ser
 1 5 10 15
 Val Pro Lys Arg Glu Glu Lys Arg Pro Tyr Gly Glu Phe Glu Arg
 20 25 30
 Gln Gln Thr Glu Gly Asn Phe Arg Gln Arg Leu Leu Gln Ser Leu
 35 40 45
 Glu Glu Phe Lys Glu Asp Ile Asp Tyr Arg His Phe Lys Asp Glu
 50 55 60
 Glu Met Thr Arg Glu Gly Asp Glu Met Glu Arg Cys Leu Glu Glu
 65 70 75
 Ile Arg Gly Leu Arg Lys Lys Phe Arg Ala Leu His Ser Asn His
 80 85 90
 Arg His Ser Arg Asp Arg Pro Tyr Pro Ile
 95 100

<210> 29
 <211> 528
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 669862CD1

<400> 29
 Met Ser Ser Pro Tyr Pro Leu Leu Leu Glu Asn Ser Ile Cys Leu
 1 5 10 15
 Phe Phe His Phe Leu Pro Asp Phe Asn Phe Thr Thr Glu Ser Asn
 20 25 30
 Lys Leu Ser Ser Glu Lys Arg Asn Tyr Glu Val Asn Ala Tyr His
 35 40 45
 Gln Glu Thr Trp Lys Arg Asn Lys Thr Phe Asn Leu Met Arg Phe
 50 55 60
 Ile Phe Arg Thr Asp Pro Gln Tyr Thr Ile Glu Phe Gly Arg Gln
 65 70 75
 Gln Arg Pro Lys Val Gly Cys Phe Ser Gln Met Ile Phe Lys Lys
 80 85 90
 His Lys Ser Leu Pro Leu His Lys Arg Asn Asn Thr Arg Glu Lys
 95 100 105
 Ser Tyr Glu Cys Lys Glu Tyr Lys Lys Gly Phe Arg Lys Tyr Leu
 110 115 120
 His Leu Thr Glu His Leu Arg Asp His Thr Gly Val Ile Pro Tyr
 125 130 135
 Glu Cys Asn Glu Cys Gly Lys Ala Phe Val Val Phe Gln His Phe

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Ile Arg His Arg	140	145	150
Lys Ile His Thr Asp	155	160	165
Asn Gly Cys Glu	170	175	180
His Gln Ile Ile	185	190	195
Cys Gly Lys Ala	200	205	210
Lys Ile His Val	215	220	225
Glu Thr Phe Arg	230	235	240
His His Gly Val	245	250	255
Phe Gly His Arg	260	265	270
Gly Glu Lys Pro	275	280	285
Arg Ser Tyr Leu	290	295	300
Lys Pro His Glu	305	310	315
Ser Ser Leu Leu	320	325	330
Tyr Asp Cys Lys	335	340	345
Leu Thr Gln His	350	355	360
Cys Lys Glu Cys	365	370	375
Gln His Gln Ile	380	385	390
Gln Cys Gly Lys	395	400	405
Gln Ser Ile His	410	415	420
Gly Lys Thr Phe	425	430	435
Ile His Thr Gly	440	445	450
Ala Phe Arg Ser	455	460	465
Thr Gly Glu Lys	470	475	480
Asn Arg Ser Asp	485	490	495
Val Lys Pro Gln	500	505	510
Cys Tyr Gln Leu	515	520	525
Leu Leu Met			

<210> 30
 <211> 350
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 1003663CD1

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<400> 30
Met His Pro Ala Ala Phe Pro Leu Pro Val Val Val Ala Ala Val
1      5      10      15
Leu Trp Gly Ala Ala Pro Thr Arg Gly Leu Ile Arg Ala Thr Ser
20     25     30
Asp His Asn Ala Ser Met Asp Phe Ala Asp Leu Pro Ala Leu Phe
35     40     45
Gly Ala Thr Leu Ser Gln Glu Gly Leu Gln Gly Phe Leu Val Glu
50     55     60
Ala His Pro Asp Asn Ala Cys Ser Pro Ile Ala Pro Pro Pro Pro
65     70     75
Ala Pro Val Asn Gly Ser Val Phe Ile Ala Leu Leu Arg Arg Phe
80     85     90
Asp Cys Asn Phe Asp Leu Lys Val Leu Asn Ala Gln Lys Ala Gly
95     100    105
Tyr Gly Ala Ala Val Val His Asn Val Asn Ser Asn Glu Leu Leu
110    115    120
Asn Met Val Trp Asn Ser Glu Glu Ile Gln Gln Gln Ile Trp Ile
125    130    135
Pro Ser Val Phe Ile Gly Glu Arg Ser Ser Glu Tyr Leu Arg Ala
140    145    150
Leu Phe Val Tyr Glu Lys Gly Ala Arg Val Leu Leu Val Pro Asp
155    160    165
Asn Thr Phe Pro Leu Gly Tyr Tyr Leu Ile Pro Phe Thr Gly Ile
170    175    180
Val Gly Leu Leu Val Leu Ala Met Gly Ala Val Met Ile Ala Arg
185    190    195
Cys Ile Gln His Arg Lys Arg Leu Gln Arg Asn Arg Leu Thr Lys
200    205    210
Glu Gln Leu Lys Gln Ile Pro Thr His Asp Tyr Gln Lys Gly Asp
215    220    225
Gln Tyr Asp Val Cys Ala Ile Cys Leu Asp Glu Tyr Glu Asp Gly
230    235    240
Asp Lys Leu Arg Val Leu Pro Cys Ala His Ala Tyr His Ser Arg
245    250    255
Cys Val Asp Pro Trp Leu Thr Gln Thr Arg Lys Thr Cys Pro Ile
260    265    270
Cys Lys Gln Pro Val His Arg Gly Pro Gly Asp Glu Asp Gln Glu
275    280    285
Glu Glu Thr Gln Gly Gln Glu Glu Gly Asp Glu Gly Glu Pro Arg
290    295    300
Asp His Pro Ala Ser Glu Arg Thr Pro Leu Leu Gly Ser Ser Pro
305    310    315
Thr Leu Pro Thr Ser Phe Gly Ser Leu Ala Pro Ala Pro Leu Val
320    325    330
Phe Pro Gly Pro Ser Thr Asp Pro Pro Leu Ser Pro Pro Ser Ser
335    340    345
Pro Val Ile Leu Val
350

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<210> 31
<211> 315
<212> PRT
<213> Homo sapiens

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<220>
<221> misc-feature
<223> Incyte ID No.: 1432557CD1

```

<400> 31
 Met Ala Ala Leu Gly Val Leu Glu Ser Asp Leu Pro Ser Ala Val
 1 5 10 15
 Thr Leu Leu Lys Asn Leu Gln Glu Gln Val Met Ala Val Thr Ala
 20 25 30
 Gln Val Lys Ser Leu Thr Gln Lys Val Gln Ala Gly Ala Tyr Pro
 35 40 45
 Thr Glu Lys Gly Leu Ser Phe Leu Glu Val Lys Asp Gln Leu Leu
 50 55 60
 Leu Met Tyr Leu Met Asp Leu Thr His Leu Ile Leu Asp Lys Ala
 65 70 75
 Ser Gly Gly Ser Leu Gln Gly His Asp Ala Val Leu Arg Leu Val
 80 85 90
 Glu Ile Arg Thr Val Leu Glu Lys Leu Arg Pro Leu Asp Gln Lys
 95 100 105
 Leu Lys Tyr Gln Ile Asp Lys Leu Ile Lys Thr Ala Val Thr Gly
 110 115 120
 Ser Leu Ser Glu Asn Asp Pro Leu Arg Phe Lys Pro His Pro Ser
 125 130 135
 Asn Met Met Ser Lys Leu Ser Ser Glu Asp Glu Glu Glu Asp Glu
 140 145 150
 Ala Glu Asp Asp Gln Ser Glu Ala Ser Gly Lys Lys Ser Val Lys
 155 160 165
 Gly Val Ser Lys Lys Tyr Val Pro Pro Arg Leu Val Pro Val His
 170 175 180
 Tyr Asp Glu Thr Glu Ala Glu Arg Glu Lys Lys Arg Leu Glu Arg
 185 190 195
 Ala Lys Arg Arg Ala Leu Ser Ser Ser Val Ile Arg Glu Leu Lys
 200 205 210
 Glu Gln Tyr Ser Asp Ala Pro Glu Glu Ile Arg Asp Ala Arg His
 215 220 225
 Pro His Val Thr Arg Gln Ser Gln Glu Asp Gln His Arg Ile Asn
 230 235 240
 Tyr Glu Glu Ser Met Met Val Arg Leu Ser Val Ser Lys Arg Glu
 245 250 255
 Lys Gly Arg Arg Lys Arg Ala Asn Val Met Ser Ser Gln Leu His
 260 265 270
 Ser Leu Thr His Phe Ser Asp Ile Ser Ala Leu Thr Gly Gly Thr
 275 280 285
 Val His Leu Asp Glu Asp Gln Asn Pro Ile Lys Lys Arg Lys Lys
 290 295 300
 Ile Pro Gln Lys Gly Arg Lys Lys Lys Gly Phe Arg Arg Arg Arg
 305 310 315

<210> 32
 <211> 120
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> 1441770CD1

<400> 32
 Met Asp Asp Ser Lys Val Val Gly Gly Lys Val Lys Lys Pro Gly
 1 5 10 15
 Lys Arg Gly Arg Lys Pro Ala Lys Ile Asp Leu Lys Ala Lys Leu
 20 25 30
 Glu Arg Ser Arg Gln Ser Ala Arg Glu Cys Arg Ala Arg Lys Lys
 35 40 45

```

Leu Arg Tyr Gln Tyr Leu Glu Glu Leu Val Ser Ser Arg Glu Arg
      50      55      60
Ala Ile Cys Ala Leu Arg Glu Glu Leu Glu Met Tyr Lys Gln Trp
      65      70      75
Cys Met Ala Met Asp Gln Gly Lys Ile Pro Ser Glu Ile Lys Ala
      80      85      90
Leu Leu Thr Gly Glu Glu Gln Asn Lys Ser Gln Gln Asn Ser Ser
      95     100     105
Arg His Thr Lys Ala Gly Lys Thr Asp Ala Asn Ser Asn Ser Trp
      110     115     120

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<210> 33
 <211> 326
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 1456684CD1

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<400> 33
Met Gln Glu Glu Pro Leu Pro Gln Gly Asn Asp Pro Glu Pro Ser
  1      5      10      15
Gly Asp Ser Pro Leu Gly Leu Cys Gln Ser Glu Cys Met Glu Met
  20      25      30
Ser Glu Val Phe Asp Asp Ala Ser Asp Gln Asp Ser Thr Asp Lys
  35      40      45
Pro Trp Arg Pro Tyr Tyr Asn Tyr Lys Pro Lys Lys Lys Ser Arg
  50      55      60
Gln Leu Lys Lys Met Arg Lys Val Asn Trp Arg Lys Glu His Gly
  65      70      75
Asn Arg Ser Pro Ser His Lys Cys Lys Tyr Pro Ala Glu Leu Asp
  80      85      90
Cys Ala Val Gly Lys Ala Pro Gln Asp Lys Pro Phe Glu Glu Glu
  95     100     105
Glu Thr Lys Glu Met Pro Lys Leu Gln Cys Glu Leu Cys Asp Gly
  110     115     120
Asp Lys Ala Val Gly Ala Gly Asn Gln Gly Arg Pro His Arg His
  125     130     135
Leu Thr Ser Arg Pro Tyr Ala Cys Glu Leu Cys Ala Lys Gln Phe
  140     145     150
Gln Ser Pro Ser Thr Leu Lys Met His Met Arg Cys His Thr Gly
  155     160     165
Glu Lys Pro Tyr Gln Cys Lys Thr Cys Gly Arg Cys Phe Ser Val
  170     175     180
Gln Gly Asn Leu Gln Lys His Glu Arg Ile His Leu Gly Leu Lys
  185     190     195
Glu Phe Val Cys Gln Tyr Cys Asn Lys Ala Phe Thr Leu Asn Glu
  200     205     210
Thr Leu Lys Ile His Glu Arg Ile His Thr Gly Glu Lys Arg Tyr
  215     220     225
His Cys Gln Phe Cys Phe Gln Arg Phe Leu Tyr Leu Ser Thr Lys
  230     235     240
Arg Asn His Glu Gln Arg His Ile Arg Glu His Asn Gly Lys Gly
  245     250     255
Tyr Ala Cys Phe Gln Cys Pro Lys Ile Cys Lys Thr Ala Ala Ala
  260     265     270
Leu Gly Met His Gln Lys Lys His Leu Phe Lys Ser Pro Ser Gln
  275     280     285

```


Gln Glu Lys Ile Gly Asp Val Cys His Glu Asn Ser Asn Pro Leu
 290 295 300
 Glu Asn Gln His Phe Ile Gly Ser Glu Asp Asn Asp Gln Lys Asp
 305 310 315
 Asn Ile Gln Thr Gly Val Glu Asn Val Val Leu
 320 325

<210> 34
 <211> 106
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 1602916CD1

<400> 34
 Met Phe Pro Trp Met Arg Pro Gln Ala Ala Pro Gly Arg Arg Arg
 1 5 10 15
 Gly Arg Gln Thr Tyr Ser Arg Phe Gln Thr Leu Glu Leu Glu Lys
 20 25 30
 Glu Phe Leu Phe Asn Pro Tyr Leu Thr Arg Lys Arg Arg Ile Glu
 35 40 45
 Val Ser His Ala Leu Ala Leu Thr Glu Arg Gln Val Lys Ile Trp
 50 55 60
 Phe Gln Asn Arg Arg Met Lys Trp Lys Lys Glu Asn Asn Lys Asp
 65 70 75
 Lys Phe Pro Val Ser Arg Gln Glu Val Lys Asp Gly Glu Thr Lys
 80 85 90
 Lys Glu Ala Gln Glu Leu Glu Glu Asp Arg Ala Glu Arg Leu Thr
 95 100 105
 Asn

<210> 35
 <211> 209
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 1692816CD1

<400> 35
 Met Asn Pro Ser Met Lys Gln Lys Gln Glu Glu Ile Lys Glu Asn
 1 5 10 15
 Ile Lys Asn Ser Ser Val Pro Arg Arg Thr Leu Lys Met Ile Gln
 20 25 30
 Pro Ser Ala Ser Gly Ser Leu Val Gly Arg Glu Asn Glu Leu Ser
 35 40 45
 Ala Gly Leu Ser Lys Arg Lys His Arg Asn Asp His Leu Thr Ser
 50 55 60
 Thr Thr Ser Ser Pro Gly Val Ile Val Pro Glu Ser Ser Glu Asn
 65 70 75
 Lys Asn Leu Gly Gly Val Thr Gln Glu Ser Phe Asp Leu Met Ile
 80 85 90
 Lys Glu Asn Pro Ser Ser Gln Tyr Trp Lys Glu Val Ala Glu Lys

Arg	Arg	Lys	Ala	95	Leu	Tyr	Glu	Ala	Leu	100	Lys	Glu	Asn	Glu	Lys	105
His	Lys	Glu	Ile	110	Glu	Gln	Lys	Asp	Asn	115	Glu	Ile	Ala	Arg	Leu	120
Lys	Glu	Asn	Lys	125	Glu	Leu	Ala	Glu	Val	130	Ala	Glu	His	Val	Gln	135
Met	Ala	Glu	Leu	140	Ile	Glu	Arg	Leu	Asn	145	Gly	Glu	Pro	Leu	Asp	150
Phe	Glu	Ser	Leu	155	Asp	Asn	Gln	Glu	Phe	160	Asp	Ser	Glu	Glu	Glu	165
Val	Glu	Asp	Ser	170	Leu	Val	Glu	Asp	Ser	175	Glu	Ile	Gly	Thr	Cys	180
Glu	Gly	Thr	Val	185	Ser	Ser	Ser	Thr	Asp	190	Ala	Lys	Pro	Cys	Ile	195
				200						205						

<210> 36
 <211> 212
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 1968191CD1

Met	Leu	Gly	Asn	Glu	Trp	Ser	Lys	Leu	Pro	Pro	Glu	Glu	Lys	Gln	
1				5					10					15	
Arg	Tyr	Leu	Asp	Glu	Ala	Asp	Arg	Asp	Lys	Glu	Arg	Tyr	Met	Lys	
				20					25					30	
Glu	Leu	Glu	Gln	Tyr	Gln	Lys	Thr	Glu	Ala	Tyr	Lys	Val	Phe	Ser	
				35					40					45	
Arg	Lys	Thr	Gln	Asp	Arg	Gln	Lys	Gly	Lys	Ser	His	Arg	Gln	Asp	
				50					55					60	
Ala	Ala	Arg	Gln	Ala	Thr	His	Asp	His	Glu	Lys	Glu	Thr	Glu	Val	
				65					70					75	
Lys	Glu	Arg	Ser	Val	Phe	Asp	Ile	Pro	Ile	Phe	Thr	Glu	Glu	Phe	
				80					85					90	
Leu	Asn	His	Ser	Lys	Ala	Arg	Glu	Ala	Glu	Leu	Arg	Gln	Leu	Arg	
				95					100					105	
Lys	Ser	Asn	Met	Glu	Phe	Glu	Glu	Arg	Asn	Ala	Ala	Leu	Gln	Lys	
				110					115					120	
His	Val	Glu	Ser	Met	Arg	Thr	Ala	Val	Glu	Lys	Leu	Glu	Val	Asp	
				125					130					135	
Val	Ile	Gln	Glu	Arg	Ser	Arg	Asn	Thr	Val	Leu	Gln	Gln	His	Leu	
				140					145					150	
Glu	Thr	Leu	Arg	Gln	Val	Leu	Thr	Ser	Ser	Phe	Ala	Ser	Met	Pro	
				155					160					165	
Leu	Pro	Gly	Ser	Gly	Glu	Thr	Pro	Thr	Val	Asp	Thr	Ile	Asp	Ser	
				170					175					180	
Tyr	Met	Asn	Arg	Leu	His	Ser	Ile	Ile	Leu	Ala	Asn	Pro	Gln	Asp	
				185					190					195	
Asn	Glu	Asn	Phe	Ile	Ala	Thr	Val	Arg	Glu	Val	Val	Asn	Arg	Leu	
				200					205					210	
Asp	Arg														

<210> 37
 <211> 359
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 2052061CD1

<400> 37
 Met Val Asp Met Asp Lys Leu Ile Asn Asn Leu Glu Val Gln Leu
 1 5 10 15
 Asn Ser Glu Gly Gly Ser Met Gln Val Phe Lys Gln Val Thr Ala
 20 25 30
 Ser Val Arg Asn Arg Asp Pro Pro Glu Ile Glu Tyr Thr Ser Asn
 35 40 45
 Met Thr Ser Pro Thr Leu Leu Asp Ala Asn Pro Met Glu Asn Pro
 50 55 60
 Ala Leu Phe Asn Asp Ile Lys Ile Glu Pro Pro Glu Glu Leu Leu
 65 70 75
 Ala Ser Asp Phe Ser Leu Pro Gln Val Glu Pro Val Asp Leu Ser
 80 85 90
 Phe His Lys Pro Lys Ala Pro Leu Gln Pro Ala Ser Met Leu Gln
 95 100 105
 Ala Pro Ile Arg Pro Pro Lys Pro Gln Ser Ser Pro Gln Thr Leu
 110 115 120
 Val Val Ser Thr Ser Thr Ser Asp Met Ser Thr Ser Ala Asn Ile
 125 130 135
 Pro Thr Val Leu Thr Pro Gly Ser Val Leu Thr Ser Ser Gln Ser
 140 145 150
 Thr Gly Ser Gln Gln Ile Leu His Val Ile His Thr Ile Pro Ser
 155 160 165
 Val Ser Leu Pro Asn Lys Met Gly Gly Leu Lys Thr Ile Pro Val
 170 175 180
 Val Val Gln Ser Leu Pro Met Val Tyr Thr Thr Leu Pro Ala Asp
 185 190 195
 Gly Gly Pro Ala Ala Ile Thr Val Pro Leu Ile Gly Gly Asp Gly
 200 205 210
 Lys Asn Ala Gly Ser Val Lys Val Asp Pro Thr Ser Met Ser Pro
 215 220 225
 Leu Glu Ile Pro Ser Asp Ser Glu Glu Ser Thr Ile Glu Ser Gly
 230 235 240
 Ser Ser Ala Leu Gln Ser Leu Gln Gly Leu Gln Gln Glu Pro Ala
 245 250 255
 Ala Met Ala Gln Met Gln Gly Glu Glu Ser Leu Asp Leu Lys Arg
 260 265 270
 Arg Arg Ile His Gln Cys Asp Phe Ala Gly Cys Ser Lys Val Tyr
 275 280 285
 Thr Lys Ser Ser His Leu Lys Ala His Arg Arg Ile His Thr Gly
 290 295 300
 Glu Lys Pro Tyr Lys Cys Thr Trp Asp Gly Cys Ser Trp Lys Phe
 305 310 315
 Ala Arg Ser Asp Glu Leu Thr Arg His Phe Arg Lys His Thr Gly
 320 325 330
 Ile Lys Pro Phe Arg Cys Thr Asp Cys Asn Arg Ser Phe Ser Arg
 335 340 345
 Ser Asp His Leu Ser Leu His Arg Arg Arg His Asp Thr Met
 350 355

<210> 38
 <211> 445
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 2056207CD1

<400> 38
 Met Val Glu Cys Ile Arg Glu Val Asn Glu Val Ile Gln Asn Pro
 1 5 10 15
 Ala Thr Ile Thr Arg Ile Leu Leu Ser His Phe Asn Trp Asp Lys
 20 25 30
 Glu Lys Leu Met Glu Arg Tyr Phe Asp Gly Asn Leu Glu Lys Leu
 35 40 45
 Phe Ala Glu Cys His Val Ile Asn Pro Ser Lys Lys Ser Arg Thr
 50 55 60
 Arg Gln Met Asn Thr Arg Ser Ser Ala Gln Asp Met Pro Cys Gln
 65 70 75
 Ile Cys Tyr Leu Asn Tyr Pro Asn Ser Tyr Phe Thr Gly Leu Glu
 80 85 90
 Cys Gly His Lys Phe Cys Met Gln Cys Trp Ser Glu Tyr Leu Thr
 95 100 105
 Thr Lys Ile Met Glu Glu Gly Met Gly Gln Thr Ile Ser Cys Pro
 110 115 120
 Ala His Gly Cys Asp Ile Leu Val Asp Asp Asn Thr Val Met Arg
 125 130 135
 Leu Ile Thr Asp Ser Lys Val Lys Leu Lys Tyr Gln His Leu Ile
 140 145 150
 Thr Asn Ser Phe Val Glu Cys Asn Arg Leu Leu Lys Trp Cys Pro
 155 160 165
 Ala Pro Asp Cys His His Val Val Lys Val Gln Tyr Pro Asp Ala
 170 175 180
 Lys Pro Val Arg Cys Lys Cys Gly Arg Gln Phe Cys Phe Asn Cys
 185 190 195
 Gly Glu Asn Trp His Asp Pro Val Lys Cys Lys Trp Leu Lys Lys
 200 205 210
 Trp Ile Lys Lys Cys Asp Asp Asp Ser Glu Thr Ser Asn Trp Ile
 215 220 225
 Ala Ala Asn Thr Lys Glu Cys Pro Lys Cys His Val Thr Ile Glu
 230 235 240
 Lys Asp Gly Gly Cys Asn His Met Val Cys Arg Asn Gln Asn Cys
 245 250 255
 Lys Ala Glu Phe Cys Trp Val Cys Leu Gly Pro Trp Glu Pro His
 260 265 270
 Gly Ser Ala Trp Tyr Asn Cys Asn Arg Tyr Asn Glu Asp Asp Ala
 275 280 285
 Lys Ala Ala Arg Asp Ala Gln Glu Arg Ser Arg Ala Ala Leu Gln
 290 295 300
 Arg Tyr Leu Phe Tyr Cys Asn Arg Tyr Met Asn His Met Gln Ser
 305 310 315
 Leu Arg Phe Glu His Lys Leu Tyr Ala Gln Val Lys Gln Lys Met
 320 325 330
 Glu Glu Met Gln Gln His Asn Met Ser Trp Ile Glu Val Gln Phe
 335 340 345
 Leu Lys Lys Ala Val Asp Val Leu Cys Gln Cys Arg Ala Thr Leu
 350 355 360
 Met Tyr Thr Tyr Val Phe Ala Phe Tyr Leu Lys Lys Asn Asn Gln
 365 370 375
 Ser Ile Ile Phe Glu Asn Asn Gln Ala Asp Leu Glu Asn Ala Thr
 380 385 390

39/91

SUBSTITUTE SHEET (RULE 26)

Glu Val Leu Ser Gly Tyr Leu Glu Arg Asp Ile Ser Gln Asp Ser
 395 400 405
 Leu Gln Asp Ile Lys Gln Lys Val Gln Asp Lys Tyr Arg Tyr Cys
 410 415 420
 Glu Ser Arg Arg Arg Val Leu Leu Gln His Val His Glu Gly Tyr
 425 430 435
 Glu Lys Asp Leu Trp Glu Tyr Ile Glu Asp
 440 445

<210> 39
 <211> 433
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 2101803CD1

<400> 39
 Met Arg Ala Glu Gly Leu Gly Gly Leu Glu Arg Phe Cys Ser Pro
 1 5 10 15
 Gly Lys Gly Arg Gly Leu Arg Ala Leu Gln Pro Phe Gln Val Gly
 20 25 30
 Asp Leu Leu Phe Ser Cys Pro Ala Tyr Ala Tyr Val Leu Thr Val
 35 40 45
 Asn Glu Arg Gly Asn His Cys Glu Tyr Cys Phe Thr Arg Lys Glu
 50 55 60
 Gly Leu Ser Lys Cys Gly Arg Cys Lys Gln Ala Phe Tyr Cys Asn
 65 70 75
 Val Glu Cys Gln Lys Glu Asp Trp Pro Met His Lys Leu Glu Cys
 80 85 90
 Ser Pro Met Val Val Phe Gly Glu Asn Trp Asn Pro Ser Glu Thr
 95 100 105
 Val Arg Leu Thr Ala Arg Ile Leu Ala Lys Gln Lys Ile His Pro
 110 115 120
 Glu Arg Thr Pro Ser Glu Lys Leu Leu Ala Val Lys Glu Phe Glu
 125 130 135
 Ser His Leu Asp Lys Leu Asp Asn Glu Lys Lys Asp Leu Ile Gln
 140 145 150
 Ser Asp Ile Ala Ala Leu His His Phe Tyr Ser Lys His Leu Glu
 155 160 165
 Phe Pro Asp Asn Asp Ser Leu Val Val Leu Phe Ala Gln Val Asn
 170 175 180
 Cys Asn Gly Phe Thr Ile Glu Asp Glu Glu Leu Ser His Leu Gly
 185 190 195
 Ser Ala Ile Phe Pro Asp Val Ala Leu Met Asn His Ser Cys Cys
 200 205 210
 Pro Asn Val Ile Val Thr Tyr Lys Gly Thr Leu Ala Glu Val Arg
 215 220 225
 Ala Val Gln Glu Ile Lys Pro Gly Glu Glu Val Phe Thr Ser Tyr
 230 235 240
 Ile Asp Leu Leu Tyr Pro Thr Glu Asp Arg Asn Asp Arg Leu Arg
 245 250 255
 Asp Ser Tyr Phe Phe Thr Cys Glu Cys Gln Glu Cys Thr Thr Lys
 260 265 270
 Asp Lys Asp Lys Ala Lys Val Glu Ile Arg Lys Leu Ser Asp Pro
 275 280 285
 Pro Lys Ala Glu Ala Ile Arg Asp Met Val Arg Tyr Ala Arg Asn
 290 295 300

Val Ile Glu Glu Phe Arg Arg Ala Lys His Tyr Lys Ser Pro Ser
 305 310 315
 Glu Leu Leu Glu Ile Cys Glu Leu Ser Gln Glu Lys Met Ser Ser
 320 325 330
 Val Phe Glu Asp Ser Asn Val Tyr Met Leu His Met Met Tyr Gln
 335 340 345
 Ala Met Gly Val Cys Leu Tyr Met Gln Asp Trp Glu Gly Ala Leu
 350 355 360
 Gln Tyr Gly Gln Lys Ile Ile Lys Pro Tyr Ser Lys His Tyr Pro
 365 370 375
 Leu Tyr Ser Leu Asn Val Ala Ser Met Trp Leu Lys Leu Gly Arg
 380 385 390
 Leu Tyr Met Gly Leu Glu His Lys Ala Ala Gly Glu Lys Ala Leu
 395 400 405
 Lys Lys Ala Ile Ala Ile Met Glu Val Ala His Gly Lys Asp His
 410 415 420
 Pro Tyr Ile Ser Glu Ile Lys Gln Glu Ile Glu Ser His
 425 430

<210> 40
 <211> 355
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 2112362CD1

<400> 40
 Met Ser Val Asn Tyr Ala Ala Gly Leu Ser Pro Tyr Ala Asp Lys
 1 5 10 15
 Gly Lys Cys Gly Leu Pro Glu Ile Phe Asp Pro Pro Glu Glu Leu
 20 25 30
 Glu Arg Lys Val Trp Glu Leu Ala Arg Leu Val Trp Gln Ser Ser
 35 40 45
 Asn Val Val Phe His Thr Gly Ala Gly Ile Ser Thr Ala Ser Gly
 50 55 60
 Ile Pro Asp Phe Arg Gly Pro His Gly Val Trp Thr Met Glu Glu
 65 70 75
 Arg Gly Leu Ala Pro Lys Phe Asp Thr Thr Phe Glu Ser Ala Arg
 80 85 90
 Pro Thr Gln Thr His Met Ala Leu Val Gln Leu Glu Arg Val Gly
 95 100 105
 Leu Leu Arg Phe Leu Val Ser Gln Asn Val Asp Gly Leu His Val
 110 115 120
 Arg Ser Gly Phe Pro Arg Asp Lys Leu Ala Glu Leu His Gly Asn
 125 130 135
 Met Phe Val Glu Glu Cys Ala Lys Cys Lys Thr Gln Tyr Val Arg
 140 145 150
 Asp Thr Val Val Gly Thr Met Gly Leu Lys Ala Thr Gly Arg Leu
 155 160 165
 Cys Thr Val Ala Lys Ala Arg Gly Leu Arg Ala Cys Arg Gly Glu
 170 175 180
 Leu Arg Asp Thr Ile Leu Asp Trp Glu Asp Ser Leu Pro Asp Arg
 185 190 195
 Asp Leu Ala Leu Ala Asp Glu Ala Ser Arg Asn Ala Asp Leu Ser
 200 205 210
 Ile Thr Leu Gly Thr Ser Leu Gln Ile Arg Pro Ser Gly Asn Leu
 215 220 225

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Pro Leu Ala Thr Lys Arg Arg Gly Gly Arg Leu Val Ile Val Asn
230 235 240
Leu Gln Pro Thr Lys His Asp Arg His Ala Asp Leu Arg Ile His
245 250 255
Gly Tyr Val Asp Glu Val Met Thr Arg Leu Met Lys His Leu Gly
260 265 270
Leu Glu Ile Pro Ala Trp Asp Gly Pro Arg Val Leu Glu Arg Ala
275 280 285
Leu Pro Pro Leu Pro Arg Pro Pro Thr Pro Lys Leu Glu Pro Lys
290 295 300
Glu Glu Ser Pro Thr Arg Ile Asn Gly Ser Ile Pro Ala Gly Pro
305 310 315
Lys Gln Glu Pro Cys Ala Gln His Asn Gly Ser Glu Pro Ala Ser
320 325 330
Pro Lys Arg Glu Arg Pro Thr Ser Pro Ala Pro His Arg Pro Pro
335 340 345
Lys Arg Val Lys Ala Lys Ala Val Pro Ser
350 355

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<210> 41
<211> 443
<212> PRT
<213> Homo sapiens

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<220>
<221> misc-feature
<223> Incyte ID No.: 2117346CD1

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<400> 41
Met Asp Arg Leu Gly Ser Phe Ser Asn Asp Pro Ser Asp Lys Pro
1 5 10 15
Pro Cys Arg Gly Cys Ser Ser Tyr Leu Met Glu Pro Tyr Ile Lys
20 25 30
Cys Ala Glu Cys Gly Pro Pro Pro Phe Phe Leu Cys Leu Gln Cys
35 40 45
Phe Thr Arg Gly Phe Glu Tyr Lys Lys His Gln Ser Asp His Thr
50 55 60
Tyr Glu Ile Met Thr Ser Asp Phe Pro Val Leu Asp Pro Ser Trp
65 70 75
Thr Ala Gln Glu Glu Met Ala Leu Leu Glu Ala Val Met Asp Cys
80 85 90
Gly Phe Gly Asn Trp Gln Asp Val Ala Asn Gln Met Cys Thr Lys
95 100 105
Thr Lys Glu Glu Cys Glu Lys His Tyr Met Lys His Phe Ile Asn
110 115 120
Asn Pro Leu Phe Ala Ser Thr Leu Leu Asn Leu Lys Gln Ala Glu
125 130 135
Glu Ala Lys Thr Ala Asp Thr Ala Ile Pro Phe His Ser Thr Asp
140 145 150
Asp Pro Pro Arg Pro Thr Phe Asp Ser Leu Leu Ser Arg Asp Met
155 160 165
Ala Gly Tyr Met Pro Ala Arg Ala Asp Phe Ile Glu Glu Phe Asp
170 175 180
Asn Tyr Ala Glu Trp Asp Leu Arg Asp Ile Asp Phe Val Glu Asp
185 190 195
Asp Ser Asp Ile Leu His Ala Leu Lys Met Ala Val Val Asp Ile
200 205 210
Tyr His Ser Arg Leu Lys Glu Arg Gln Arg Arg Lys Lys Ile Ile
215 220 225

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Arg Asp His Gly Leu Ile Asn Leu Arg Lys Phe Gln Leu Met Glu
230 235 240
Arg Arg Tyr Pro Lys Glu Val Gln Asp Leu Tyr Glu Thr Met Arg
245 250 255
Arg Phe Ala Arg Ile Val Gly Pro Val Glu His Asp Lys Phe Ile
260 265 270
Glu Ser His Ala Leu Glu Phe Glu Leu Arg Arg Glu Ile Lys Arg
275 280 285
Leu Gln Glu Tyr Arg Thr Ala Gly Ile Thr Asn Phe Cys Ser Ala
290 295 300
Arg Thr Tyr Asp His Leu Lys Lys Thr Arg Glu Glu Glu Arg Leu
305 310 315
Lys Arg Thr Met Leu Ser Glu Val Leu Gln Tyr Ile Gln Asp Ser
320 325 330
Ser Ala Cys Gln Gln Trp Leu Arg Arg Gln Ala Asp Ile Asp Ser
335 340 345
Gly Leu Ser Pro Ser Ile Pro Met Ala Ser Asn Ser Gly Arg Arg
350 355 360
Ser Ala Pro Pro Leu Asn Leu Thr Gly Leu Pro Gly Thr Glu Lys
365 370 375
Leu Asn Glu Lys Glu Lys Glu Leu Cys Gln Met Val Arg Leu Val
380 385 390
Pro Gly Ala Tyr Leu Glu Tyr Lys Ser Ala Leu Leu Asn Glu Cys
395 400 405
Asn Lys Gln Gly Gly Leu Arg Leu Ala Gln Ala Arg Ala Leu Ile
410 415 420
Lys Ile Asp Val Asn Lys Thr Arg Lys Ile Tyr Asp Phe Leu Ile
425 430 435
Arg Glu Gly Tyr Ile Thr Lys Gly
440

```

<210> 42
 <211> 164
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 2119917CD1

```

<400> 42
Met Thr Ala Ser Ala Gln Pro Arg Gly Arg Arg Pro Gly Val Gly
1 5 10 15
Val Gly Val Val Val Thr Ser Cys Lys His Pro Arg Cys Val Leu
20 25 30
Leu Gly Lys Arg Lys Gly Ser Val Gly Ala Gly Ser Phe Gln Leu
35 40 45
Pro Gly Gly His Leu Glu Phe Gly Glu Thr Trp Glu Glu Cys Ala
50 55 60
Gln Arg Glu Thr Trp Glu Glu Ala Ala Leu His Leu Lys Asn Val
65 70 75
His Phe Ala Ser Val Val Asn Ser Phe Ile Glu Lys Glu Asn Tyr
80 85 90
His Tyr Val Thr Ile Leu Met Lys Gly Glu Val Asp Val Thr His
95 100 105
Asp Ser Glu Pro Lys Asn Val Glu Pro Glu Lys Asn Glu Ser Trp
110 115 120
Glu Trp Val Pro Trp Glu Glu Leu Pro Pro Leu Asp Gln Leu Phe
125 130 135

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Trp Gly Leu Arg Cys Leu Lys Glu Gln Gly Tyr Asp Pro Phe Lys
 140 145 150
 Glu Asp Leu Asn His Leu Val Gly Tyr Lys Gly Asn His Leu
 155 160

<210> 43
 <211> 215
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 2123456CD1

<400> 43
 Met Leu Gly Ala Glu Trp Ser Lys Leu Gln Pro Thr Glu Lys Gln
 1 5 10 15
 Arg Tyr Leu Asp Glu Ala Glu Arg Glu Lys Gln Gln Tyr Met Lys
 20 25 30
 Glu Leu Arg Ala Tyr Gln Gln Ser Glu Ala Tyr Lys Met Cys Thr
 35 40 45
 Glu Lys Ile Gln Glu Lys Lys Ile Lys Lys Glu Asp Ser Ser Ser
 50 55 60
 Gly Leu Met Asn Thr Leu Leu Asn Gly His Lys Gly Gly Asp Cys
 65 70 75
 Asp Gly Phe Ser Thr Phe Asp Val Pro Ile Phe Thr Glu Glu Phe
 80 85 90
 Leu Asp Gln Asn Lys Ala Arg Glu Ala Glu Leu Arg Arg Leu Arg
 95 100 105
 Lys Met Asn Val Ala Phe Glu Glu Gln Asn Ala Val Leu Gln Arg
 110 115 120
 His Thr Gln Ser Met Ser Ser Ala Arg Glu Arg Leu Glu Gln Glu
 125 130 135
 Leu Ala Leu Glu Glu Arg Arg Thr Leu Ala Leu Gln Gln Gln Leu
 140 145 150
 Gln Ala Val Arg Gln Ala Leu Thr Ala Ser Phe Ala Ser Leu Pro
 155 160 165
 Val Pro Gly Thr Gly Glu Thr Pro Thr Leu Gly Thr Leu Asp Phe
 170 175 180
 Tyr Met Ala Arg Leu His Gly Ala Ile Glu Arg Asp Pro Ala Gln
 185 190 195
 His Glu Lys Leu Ile Val Arg Ile Lys Glu Ile Leu Ala Gln Val
 200 205 210
 Ala Ser Glu His Leu
 215

<210> 44
 <211> 539
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 2148792CD1

<400> 44

Met	Ala	Ala	Leu	Phe	Leu	Ser	Ala	Pro	Pro	Gln	Ala	Glu	Val	Thr	
1				5					10					15	
Phe	Glu	Asp	Val	Ala	Val	Tyr	Leu	Ser	Arg	Glu	Glu	Trp	Gly	Arg	
			20						25					30	
Leu	Gly	Pro	Ala	Gln	Arg	Gly	Leu	Tyr	Arg	Asp	Val	Met	Leu	Glu	
			35						40					45	
Thr	Tyr	Gly	Asn	Leu	Val	Ser	Leu	Gly	Val	Gly	Pro	Ala	Gly	Pro	
			50						55					60	
Lys	Pro	Gly	Val	Ile	Ser	Gln	Leu	Glu	Arg	Gly	Asp	Glu	Pro	Trp	
			65						70					75	
Val	Leu	Asp	Val	Gln	Gly	Thr	Ser	Gly	Lys	Glu	His	Leu	Arg	Val	
			80						85					90	
Asn	Ser	Pro	Ala	Leu	Gly	Thr	Arg	Thr	Glu	Tyr	Lys	Glu	Leu	Thr	
			95						100					105	
Ser	Gln	Glu	Thr	Phe	Gly	Glu	Glu	Asp	Pro	Gln	Gly	Ser	Glu	Pro	
			110						115					120	
Val	Glu	Ala	Cys	Asp	His	Ile	Ser	Lys	Ser	Glu	Gly	Ser	Leu	Glu	
			125						130					135	
Lys	Leu	Val	Glu	Gln	Arg	Gly	Pro	Arg	Ala	Val	Thr	Leu	Thr	Asn	
			140						145					150	
Gly	Glu	Ser	Ser	Arg	Glu	Ser	Gly	Gly	Asn	Leu	Arg	Leu	Leu	Ser	
			155						160					165	
Arg	Pro	Val	Pro	Asp	Gln	Arg	Pro	His	Lys	Cys	Asp	Ile	Cys	Glu	
			170						175					180	
Gln	Ser	Phe	Glu	Gln	Arg	Ser	Tyr	Leu	Asn	Asn	His	Lys	Arg	Val	
			185						190					195	
His	Arg	Ser	Lys	Lys	Thr	Asn	Thr	Val	Arg	Asn	Ser	Gly	Glu	Ile	
			200						205					210	
Phe	Ser	Ala	Asn	Leu	Val	Val	Lys	Glu	Asp	Gln	Lys	Ile	Pro	Thr	
			215						220					225	
Gly	Lys	Lys	Leu	His	Tyr	Cys	Ser	Tyr	Cys	Gly	Lys	Thr	Phe	Arg	
			230						235					240	
Tyr	Ser	Ala	Asn	Leu	Val	Lys	His	Gln	Arg	Leu	His	Thr	Glu	Glu	
			245						250					255	
Lys	Pro	Tyr	Lys	Cys	Asp	Glu	Cys	Gly	Lys	Ala	Phe	Ser	Gln	Ser	
			260						265					270	
Cys	Glu	Phe	Ile	Asn	His	Arg	Arg	Met	His	Ser	Gly	Glu	Ile	Pro	
			275						280					285	
Tyr	Arg	Cys	Asp	Glu	Cys	Gly	Lys	Thr	Phe	Thr	Arg	Arg	Pro	Asn	
			290						295					300	
Leu	Met	Lys	His	Gln	Arg	Ile	His	Thr	Gly	Glu	Lys	Pro	Tyr	Lys	
			305						310					315	
Cys	Gly	Glu	Cys	Gly	Lys	His	Phe	Ser	Ala	Tyr	Ser	Ser	Leu	Ile	
			320						325					330	
Tyr	His	Gln	Arg	Ile	His	Thr	Gly	Glu	Lys	Pro	Tyr	Lys	Cys	Asn	
			335						340					345	
Asp	Cys	Gly	Lys	Ala	Phe	Ser	Asp	Gly	Ser	Ile	Leu	Ile	Arg	His	
			350						355					360	
Arg	Arg	Thr	His	Thr	Gly	Glu	Lys	Pro	Phe	Glu	Cys	Lys	Glu	Cys	
			365						370					375	
Gly	Lys	Gly	Phe	Thr	Gln	Ser	Ser	Asn	Leu	Ile	Gln	His	Gln	Arg	
			380						385					390	
Ile	His	Thr	Gly	Glu	Lys	Pro	Tyr	Lys	Cys	Asn	Glu	Cys	Glu	Lys	
			395						400					405	
Ala	Phe	Ile	Gln	Lys	Thr	Lys	Leu	Val	Glu	His	Gln	Arg	Ser	His	
			410						415					420	
Thr	Gly	Glu	Lys	Pro	Tyr	Glu	Cys	Asn	Asp	Cys	Gly	Lys	Val	Phe	
			425						430					435	
Ser	Gln	Ser	Thr	His	Leu	Ile	Gln	His	Gln	Arg	Ile	His	Thr	Gly	
			440						445					450	
Glu	Lys	Pro	Tyr	Lys	Cys	Ser	Glu	Cys	Gly	Lys	Ala	Phe	His	Asn	
			455						460					465	

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Ser Ser Arg Leu Ile His His Gln Arg Leu His His Gly Glu Lys
      470                      475                      480
Pro Tyr Arg Cys Ser Asp Cys Lys Lys Ala Phe Ser Gln Ser Thr
      485                      490                      495
Tyr Leu Ile Gln His Arg Arg Ile His Thr Gly Glu Lys Pro Tyr
      500                      505                      510
Lys Cys Ser Glu Cys Gly Lys Ala Phe Arg His Ser Ser Asn Met
      515                      520                      525
Cys Gln His Gln Arg Ile His Leu Arg Glu Asp Phe Ser Met
      530                      535

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<210> 45
 <211> 182
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 2751943CD1

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<400> 45
Met Ala Arg Leu Leu Trp Leu Leu Arg Gly Leu Thr Leu Gly Thr
  1          5          10          15
Ala Pro Arg Arg Ala Val Arg Gly Gln Ala Gly Gly Gly Gly Pro
      20          25          30
Gly Thr Gly Pro Gly Leu Gly Glu Ala Gly Ser Leu Ala Thr Cys
      35          40          45
Glu Leu Pro Leu Ala Lys Ser Glu Trp Gln Lys Lys Leu Thr Pro
      50          55          60
Glu Gln Phe Tyr Val Thr Arg Glu Lys Gly Thr Glu Pro Pro Phe
      65          70          75
Ser Gly Ile Tyr Leu Asn Asn Lys Glu Ala Gly Met Tyr His Cys
      80          85          90
Val Cys Cys Asp Ser Pro Leu Phe Ser Ser Glu Lys Lys Tyr Cys
      95          100         105
Ser Gly Thr Gly Trp Pro Ser Phe Ser Glu Ala His Gly Thr Ser
      110         115         120
Gly Ser Asp Glu Ser His Thr Gly Ile Leu Arg Arg Leu Asp Thr
      125         130         135
Ser Leu Gly Ser Ala Arg Thr Glu Val Val Cys Lys Gln Cys Glu
      140         145         150
Ala His Leu Gly His Val Phe Pro Asp Gly Pro Gly Pro Asn Gly
      155         160         165

Gln Arg Phe Cys Ile Asn Ser Val Ala Leu Lys Phe Lys Pro Arg
      170         175         180
Lys His

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<210> 46
 <211> 534
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 3128913CD1

<400> 46
 Met Ala Val Glu Ser Gly Val Ile Ser Thr Leu Ile Pro Gln Asp
 1 5 10 15
 Pro Pro Glu Gln Glu Leu Ile Leu Val Lys Val Glu Asp Asn Phe
 20 25 30
 Ser Trp Asp Glu Lys Phe Lys Gln Asn Gly Ser Thr Gln Ser Cys
 35 40 45
 Gln Glu Leu Phe Arg Gln Gln Phe Arg Lys Phe Cys Tyr Gln Glu
 50 55 60
 Thr Pro Gly Pro Arg Glu Ala Leu Ser Arg Leu Gln Glu Leu Cys
 65 70 75
 Tyr Gln Trp Leu Met Pro Glu Leu His Thr Lys Glu Gln Ile Leu
 80 85 90
 Glu Leu Leu Val Leu Glu Gln Phe Leu Ser Ile Leu Pro Glu Glu
 95 100 105
 Leu Gln Ile Trp Val Gln Gln His Asn Pro Glu Ser Gly Glu Glu
 110 115 120
 Ala Val Thr Leu Leu Glu Asp Leu Glu Arg Glu Phe Asp Asp Pro
 125 130 135
 Gly Gln Gln Val Pro Ala Ser Pro Gln Gly Pro Ala Val Pro Trp
 140 145 150
 Lys Asp Leu Thr Cys Leu Arg Ala Ser Gln Glu Ser Thr Asp Ile
 155 160 165
 His Leu Gln Pro Leu Lys Thr Gln Leu Lys Ser Trp Lys Pro Cys
 170 175 180
 Leu Ser Pro Lys Ser Asp Cys Glu Asn Ser Glu Thr Ala Thr Lys
 185 190 195
 Glu Gly Ile Ser Glu Glu Lys Ser Gln Gly Leu Pro Gln Glu Pro
 200 205 210
 Ser Phe Arg Gly Ile Ser Glu His Glu Ser Asn Leu Val Trp Lys
 215 220 225
 Gln Gly Ser Ala Thr Gly Glu Lys Leu Arg Ser Pro Ser Gln Gly
 230 235 240
 Gly Ser Phe Ser Gln Val Ile Phe Thr Asn Lys Ser Leu Gly Lys
 245 250 255
 Arg Asp Leu Tyr Asp Glu Ala Glu Arg Cys Leu Ile Leu Thr Thr
 260 265 270
 Asp Ser Ile Met Cys Gln Lys Val Pro Pro Glu Glu Arg Pro Tyr
 275 280 285
 Arg Cys Asp Val Cys Gly His Ser Phe Lys Gln His Ser Ser Leu
 290 295 300
 Thr Gln His Gln Arg Ile His Thr Gly Glu Lys Pro Tyr Lys Cys
 305 310 315
 Asn Gln Cys Gly Lys Ala Phe Ser Leu Arg Ser Tyr Leu Ile Ile
 320 325 330
 His Gln Arg Ile His Ser Gly Glu Lys Ala Tyr Glu Cys Ser Glu
 335 340 345
 Cys Gly Lys Ala Phe Asn Gln Ser Ser Ala Leu Ile Arg His Arg
 350 355 360
 Lys Ile His Thr Gly Glu Lys Ala Cys Lys Cys Asn Glu Cys Gly
 365 370 375
 Lys Ala Phe Ser Gln Ser Ser Tyr Leu Ile Ile His Gln Arg Ile
 380 385 390
 His Thr Gly Glu Lys Pro Tyr Glu Cys Asn Glu Cys Gly Lys Thr
 395 400 405
 Phe Ser Gln Ser Ser Lys Leu Ile Arg His Gln Arg Ile His Thr
 410 415 420
 Gly Glu Arg Pro Tyr Glu Cys Asn Glu Cys Gly Lys Ala Phe Arg
 425 430 435
 Gln Ser Ser Glu Leu Ile Thr His Gln Arg Ile His Ser Gly Glu
 440 445 450
 Lys Pro Tyr Glu Cys Ser Glu Cys Gly Lys Ala Phe Ser Leu Ser

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          455          460          465
Ser Asn Leu Ile Arg His Gln Arg Ile His Ser Gly Glu Glu Pro
          470          475          480
Tyr Gln Cys Asn Glu Cys Gly Lys Thr Phe Lys Arg Ser Ser Ala
          485          490          495
Leu Val Gln His Gln Arg Ile His Ser Gly Asp Glu Ala Tyr Ile
          500          505          510
Cys Asn Glu Cys Gly Lys Ala Phe Arg His Arg Ser Val Leu Met
          515          520          525

Arg His Gln Arg Val His Thr Ile Lys
          530

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<210> 47
<211> 206
<212> PRT
<213> Homo sapiens

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<220>
<221> misc-feature
<223> Incyte ID No.: 3282941CD1

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<400> 47
Met Ser Thr Gly Ser Val Ser Asp Pro Glu Glu Met Glu Leu Arg
 1          5          10          15
Gly Leu Gln Arg Glu Tyr Pro Val Pro Ala Ser Lys Arg Pro Pro
          20          25          30
Leu Arg Gly Val Glu Arg Ser Tyr Ala Ser Pro Ser Asp Asn Ser
          35          40          45
Ser Ala Glu Glu Glu Asp Pro Asp Gly Glu Glu Arg Cys Ala
          50          55          60
Leu Gly Thr Ala Gly Ser Ala Glu Gly Cys Lys Arg Lys Arg Pro
          65          70          75
Arg Val Ala Gly Gly Gly Gly Ala Gly Gly Ser Ala Gly Gly Gly
          80          85          90
Gly Lys Lys Pro Leu Pro Ala Lys Gly Ser Ala Ala Glu Cys Lys
          95          100          105
Gln Ser Gln Arg Asn Ala Ala Asn Ala Arg Glu Arg Ala Arg Met
          110          115          120
Arg Val Leu Ser Lys Ala Phe Ser Arg Leu Lys Thr Ser Leu Pro
          125          130          135
Trp Val Pro Pro Asp Thr Lys Leu Ser Lys Leu Asp Thr Leu Arg
          140          145          150
Leu Ala Ser Ser Tyr Ile Ala His Leu Arg Gln Leu Leu Gln Glu
          155          160          165
Asp Arg Tyr Glu Asn Gly Tyr Val His Pro Val Asn Leu Thr Trp
          170          175          180
Pro Phe Val Val Ser Gly Arg Pro Asp Ser Asp Thr Lys Glu Val
          185          190          195
Ser Ala Ala Asn Arg Leu Cys Gly Thr Thr Ala
          200          205

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<210> 48
<211> 172
<212> PRT
<213> Homo sapiens

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<220>
 <221> misc-feature
 <223> Incyte ID No.: 3286656CD1

<400> 48
 Met Glu Ser Val Thr Phe Glu Asp Val Ala Val Glu Phe Ile Gln
 1 5 10 15
 Glu Trp Ala Leu Leu Asp Ser Ala Arg Arg Ser Leu Cys Lys Tyr
 20 25 30
 Arg Met Leu Asp Gln Cys Arg Thr Leu Ala Ser Arg Gly Thr Pro
 35 40 45
 Pro Cys Lys Pro Ser Cys Val Ser Gln Leu Gly Gln Arg Ala Glu
 50 55 60
 Pro Lys Ala Thr Glu Arg Gly Ile Leu Arg Ala Thr Gly Val Ala
 65 70 75
 Trp Glu Ser Gln Leu Lys Pro Glu Glu Leu Pro Ser Met Gln Asp
 80 85 90
 Leu Leu Glu Glu Ala Ser Ser Arg Asp Met Gln Met Gly Pro Gly
 95 100 105
 Leu Phe Leu Arg Met Gln Leu Val Pro Ser Ile Glu Glu Arg Glu
 110 115 120
 Thr Pro Leu Thr Arg Glu Asp Arg Pro Ala Leu Gln Glu Pro Pro
 125 130 135
 Trp Ser Leu Gly Cys Thr Gly Leu Lys Ala Ala Met Gln Ile Gln
 140 145 150
 Arg Val Val Ile Pro Val Pro Thr Leu Gly His Arg Asn Pro Trp
 155 160 165
 Val Ala Arg Asp Ser Ala Met
 170

<210> 49
 <211> 275
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 3490802CD1

<400> 49
 Met Gly Pro Leu Gln Phe Arg Asp Val Ala Ile Glu Phe Ser Leu
 1 5 10 15
 Glu Glu Trp His Cys Leu Asp Thr Ala Gln Arg Asn Leu Tyr Arg
 20 25 30
 Asp Val Met Leu Glu Asn Tyr Arg Asn Leu Val Phe Leu Gly Ile
 35 40 45
 Val Val Ser Lys Pro Asp Leu Val Thr Cys Leu Glu Gln Gly Lys
 50 55 60
 Lys Pro Leu Thr Met Glu Arg His Glu Met Ile Ala Lys Pro Pro
 65 70 75
 Val Met Ser Ser His Phe Ala Gln Asp Leu Trp Pro Glu Asn Ile
 80 85 90
 Gln Asn Ser Phe Gln Ile Gly Met Leu Arg Arg Tyr Glu Glu Cys
 95 100 105
 Arg His Asp Asn Leu Gln Leu Lys Lys Gly Cys Lys Ser Val Gly
 110 115 120
 Glu His Lys Val His Lys Gly Gly Tyr Asn Gly Leu Asn Gln Cys
 125 130 135
 Leu Thr Thr Thr Gln Lys Glu Ile Phe Gln Cys Asp Lys Tyr Gly

Lys Val Phe His	140	145	150
Lys Phe Ser Asn Ser	155	160	165
His Thr Gly Ile	170	175	180
Phe Lys Arg Ser	185	190	195
Gly Glu Lys Pro	200	205	210
Gln Ser Ser Asn	215	220	225
Lys Pro Tyr Lys	230	235	240
Ser Asp Leu Asn	245	250	255
Tyr Ile Val Lys	260	265	270
Leu Ile Ser Ile	275		

<210> 50
 <211> 236
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 3507366CD1

<400> 50

Met Asp Lys Arg Tyr Leu Gln Phe Asp Ile Lys Ala Phe Val Glu	1	5	10	15
Asn Asn Pro Ala Ile Lys Trp Cys Pro Thr Pro Gly Cys Asp Arg	20	25	30	35
Ala Val Arg Leu Thr Lys Gln Gly Ser Asn Thr Ser Gly Ser Asp	40	45	50	55
Thr Leu Ser Phe Pro Leu Leu Arg Ala Pro Ala Val Asp Cys Gly	60	65	70	75
Lys Gly His Leu Phe Cys Trp Glu Cys Leu Gly Glu Ala His Glu	80	85	90	95
Pro Cys Asp Cys Gln Thr Trp Lys Asn Trp Leu Gln Lys Ile Thr	100	105	110	115
Glu Met Lys Pro Glu Glu Leu Val Gly Val Ser Glu Ala Tyr Glu	120	125	130	135
Asp Ala Ala Asn Cys Leu Trp Leu Leu Thr Asn Ser Lys Pro Cys	140	145	150	155
Ala Asn Cys Lys Ser Pro Ile Gln Lys Asn Glu Gly Cys Asn His	160	165	170	175
Met Gln Cys Ala Lys Cys Lys Tyr Asp Phe Cys Trp Ile Cys Leu	180	185	190	195
Glu Glu Trp Lys Lys His Ser Ser Ser Thr Gly Gly Tyr Tyr Arg	200	205	210	215
Cys Thr Arg Tyr Glu Val Ile Gln His Val Glu Glu Gln Ser Lys	220	225	230	235
Glu Met Thr Val Glu Ala Glu Lys Lys His Lys Arg Phe Gln Glu	240	245	250	255
Leu Asp Arg Phe Met His Tyr Tyr Thr Arg Phe Lys Asn His Glu	260	265	270	275
His Ser Tyr Gln Leu Glu Gln Arg Leu Leu Lys Thr Ala Lys Glu				

215
 Lys Met Glu Gln Met Ser Arg Val Ser Lys Asn 220
 230 235 225

<210> 51
 <211> 214
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 3573060CD1

<400> 51
 Met Asn Leu Ser Ser Ala Ser Ser Thr Glu Glu Lys Ala Val Thr
 1 5 10 15
 Thr Val Leu Trp Gly Cys Glu Leu Ser Gln Glu Arg Arg Thr Trp
 20 25 30
 Thr Phe Arg Pro Gln Leu Glu Gly Lys Gln Ser Cys Arg Leu Leu
 35 40 45
 Leu His Thr Ile Cys Leu Gly Glu Lys Ala Lys Glu Glu Met His
 50 55 60
 Arg Val Glu Ile Leu Pro Pro Ala Asn Gln Glu Asp Lys Lys Met
 65 70 75
 Gln Pro Val Thr Ile Ala Ser Leu Gln Ala Ser Val Leu Pro Met
 80 85 90
 Val Ser Met Val Gly Val Gln Leu Ser Pro Pro Val Thr Phe Gln
 95 100 105
 Leu Arg Ala Gly Ser Gly Pro Val Phe Leu Ser Gly Gln Glu Arg
 110 115 120
 Tyr Glu Ala Ser Asp Leu Thr Trp Glu Glu Glu Glu Glu Glu
 125 130 135
 Gly Glu Glu Glu Glu Glu Glu Glu Asp Asp Glu Asp Glu Asp
 140 145 150
 Ala Asp Ile Ser Leu Glu Glu Gln Ser Pro Val Lys Gln Val Lys
 155 160 165
 Arg Leu Val Pro Gln Lys Gln Ala Ser Val Ala Lys Lys Lys Lys
 170 175 180
 Leu Glu Lys Glu Glu Glu Ile Arg Ala Ser Val Arg Asp Lys
 185 190 195
 Ser Pro Val Lys Lys Ala Lys Ala Thr Ala Arg Ala Lys Lys Pro
 200 205 210
 Gly Phe Lys Lys

<210> 52
 <211> 396
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 3573661CD1

<400> 52
 Met Asn Phe Thr Val Gly Phe Lys Pro Leu Leu Gly Asp Ala His

1	5	10	15
Ser Met Asp Asn Leu	Glu Lys Gln Leu	Ile Cys Pro Ile Cys	Leu
20	25	30	
Glu Met Phe Ser Lys	Pro Val Val Ile	Leu Pro Cys Gln His	Asn
35	40	45	
Leu Cys Arg Lys Cys	Ala Asn Asp Val	Phe Gln Ala Ser Asn	Pro
50	55	60	
Leu Trp Gln Ser Arg	Gly Ser Thr Thr	Val Ser Ser Gly Gly	Arg
65	70	75	
Phe Arg Cys Pro Ser	Cys Arg His Glu	Val Val Leu Asp Arg	His
80	85	90	
Gly Val Tyr Gly Leu	Gln Arg Asn Val	Leu Val Glu Asn Ile	Ile
95	100	105	
Asp Ile Tyr Lys Gln	Glu Ser Ser Lys	Pro Leu His Ser Lys	Ala
110	115	120	
Glu Gln His Leu Met	Cys Glu Glu His	Glu Glu Glu Lys Ile	Asn
125	130	135	
Ile Tyr Cys Leu Ser	Cys Glu Val Pro	Thr Cys Ser Leu Cys	Lys
140	145	150	
Val Phe Gly Ala His	Lys Asp Cys Glu	Val Ala Pro Leu Pro	Thr
155	160	165	
Ile Tyr Lys Arg Gln	Lys Ser Glu Leu	Ser Asp Gly Ile Ala	Met
170	175	180	
Leu Val Ala Gly Asn	Asp Arg Val Gln	Ala Val Ile Thr Gln	Met
185	190	195	
Glu Glu Val Cys Gln	Thr Ile Glu Asp	Asn Ser Arg Arg Gln	Lys
200	205	210	
Gln Leu Leu Asn Gln	Arg Phe Glu Ser	Leu Cys Ala Val Leu	Glu
215	220	225	
Glu Arg Lys Gly Glu	Leu Leu Gln Ala	Leu Ala Arg Glu Gln	Glu
230	235	240	
Glu Lys Leu Gln Arg	Val Arg Gly Leu	Ile Arg Gln Tyr Gly	Asp
245	250	255	
His Leu Glu Ala Ser	Ser Lys Leu Val	Glu Ser Ala Ile Gln	Ser
260	265	270	
Met Glu Glu Pro Gln	Met Ala Leu Tyr	Leu Gln Gln Ala Lys	Glu
275	280	285	
Leu Ile Asn Lys Val	Gly Ala Met Ser	Lys Val Glu Leu Ala	Gly
290	295	300	
Arg Pro Glu Pro Gly	Tyr Glu Ser Met	Glu Gln Phe Thr Val	Arg
305	310	315	
Val Glu His Val Ala	Glu Met Leu Arg	Thr Ile Asp Phe Gln	Pro
320	325	330	
Gly Ala Ser Gly Gly	Gly Arg Gly Gly	Gly Pro Arg Arg Lys	Lys
335	340	345	
Arg Ala Thr Arg Gly	Pro Glu Glu Lys	Thr Ala Arg Met Gly	Pro
350	355	360	
Tyr Arg Pro Leu Arg	Pro Asn Pro Asp	Pro Leu Leu Arg Lys	Ser
365	370	375	
Pro Arg Arg Leu Arg	Ile Ser Gly Gly	Arg Asn Ser Cys Arg	Lys
380	385	390	
Lys Thr Pro Ala Ser	Phe		
395			

<210> 53
 <211> 486
 <212> PRT
 <213> Homo sapiens

<220>

<221> misc-feature

<223> Incyte ID No.: 3633422CD1

<400> 53

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Met Arg Arg Leu Val His..Asp Leu Leu Pro Pro Glu Val Cys Ser
 1           5           10           15
Leu Leu Asn Pro Ala Ala Ile Tyr Ala Asn Asn Glu Ile Ser Leu
          20           25           30
Arg Asp Val Glu Val Tyr Gly Phe Asp Tyr Asp Tyr Thr Leu Ala
          35           40           45
Gln Tyr Ala Asp Ala Leu His Pro Glu Ile Phe Ser Thr Ala Arg
          50           55           60
Asp Ile Leu Ile Glu His Tyr Lys Tyr Pro Glu Gly Ile Arg Lys
          65           70           75
Tyr Asp Tyr Asn Pro Ser Phe Ala Ile Arg Gly Leu His Tyr Asp
          80           85           90
Ile Gln Lys Ser Leu Leu Met Lys Ile Asp Ala Phe His Tyr Val
          95          100          105
Gln Leu Gly Thr Ala Tyr Arg Gly Leu Gln Pro Val Pro Asp Glu
          110          115          120
Glu Val Ile Glu Leu Tyr Gly Gly Thr Gln His Ile Pro Leu Tyr
          125          130          135
Gln Met Ser Gly Phe Tyr Gly Lys Gly Pro Ser Ile Lys Gln Phe
          140          145          150
Met Asp Ile Phe Ser Leu Pro Glu Met Ala Leu Leu Ser Cys Val
          155          160          165
Val Asp Tyr Phe Leu Gly His Ser Leu Glu Phe Asp Gln Ala His
          170          175          180
Leu Tyr Lys Asp Val Thr Asp Ala Ile Arg Asp Val His Val Lys
          185          190          195
Gly Leu Met Tyr Gln Trp Ile Glu Gln Asp Met Glu Lys Tyr Ile
          200          205          210
Leu Arg Gly Asp Glu Thr Phe Ala Val Leu Ser Arg Leu Val Ala
          215          220          225
His Gly Lys Gln Leu Phe Leu Ile Thr Asn Ser Pro Phe Ser Phe
          230          235          240
Val Asp Lys Gly Met Arg His Met Val Gly Pro Asp Trp Arg Gln
          245          250          255
Leu Phe Asp Val Val Ile Val Gln Ala Asp Lys Pro Ser Phe Phe
          260          265          270
Thr Asp Arg Arg Lys Pro Phe Arg Lys Leu Asp Glu Lys Gly Ser
          275          280          285
Leu Gln Trp Asp Arg Ile Thr Arg Leu Glu Lys Gly Lys Ile Tyr
          290          295          300
Arg Gln Gly Asn Leu Phe Asp Phe Leu Arg Leu Thr Glu Trp Arg
          305          310          315
Gly Pro Arg Val Leu Tyr Phe Gly Asp His Leu Tyr Ser Asp Leu
          320          325          330
Ala Asp Leu Met Leu Arg His Gly Trp Arg Thr Gly Ala Ile Ile
          335          340          345
Pro Glu Leu Glu Arg Glu Ile Arg Ile Ile Asn Thr Glu Gln Tyr
          350          355          360
Met His Ser Leu Thr Trp Gln Gln Ala Leu Thr Gly Leu Leu Glu
          365          370          375
Arg Met Gln Thr Tyr Gln Asp Ala Glu Ser Arg Gln Val Leu Ala
          380          385          390
Ala Trp Met Lys Glu Arg Gln Glu Leu Arg Cys Ile Thr Lys Ala
          395          400          405
Leu Phe Asn Ala Gln Phe Gly Ser Ile Phe Arg Thr Phe His Asn
          410          415          420
Pro Thr Tyr Phe Ser Arg Arg Leu Val Arg Phe Ser Asp Leu Tyr

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	425		430		435
Met Ala Ser Leu	Ser Cys Leu Leu Asn	Tyr Arg Val Asp Phe	Thr		
	440		445		450
Phe Tyr Pro Arg	Arg Thr Pro Leu Gln	His Glu Ala Pro Leu	Trp		
	455		460		465
Met Asp Gln Leu	Cys Thr Gly Cys Met	Lys Thr Pro Phe Leu	Gly		
	470		475		480
Asp Met Ala His	Ile Arg				
	485				

<210> 54
 <211> 555
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 3993377CD1

<400> 54

Met Gly Ala Glu Asp	Lys Leu Pro Leu Glu Asp Ser Pro Val Ile	
1	5	10 15
Ala Ala Leu Asp Cys	Pro Ser Leu Asn Asn Ala Thr Ala Phe Ser	
	20	25 30
Leu Leu Ala Asp Asp	Ser Gln Thr Ser Thr Ser Ile Phe Ala Ser	
	35	40 45
Pro Thr Ser Pro Pro	Val Leu Gly Glu Ser Val Leu Gln Asp Asn	
	50	55 60
Ser Phe Asp Leu Asn	Asn Gly Ser Asp Ala Glu Gln Glu Glu Met	
	65	70 75
Glu Thr Gln Ser Ser	Asp Phe Pro Pro Ser Leu Thr Gln Pro Ala	
	80	85 90
Pro Asp Gln Ser Ser	Thr Ile Gln Leu His Pro Ala Thr Ser Pro	
	95	100 105
Ala Val Ser Pro Thr	Thr Ser Pro Ala Val Ser Leu Val Val Ser	
	110	115 120
Pro Ala Ala Ser Pro	Glu Ile Ser Pro Glu Val Cys Pro Ala Ala	
	125	130 135
Ser Thr Val Val Ser	Pro Ala Val Phe Ser Val Val Ser Pro Ala	
	140	145 150
Ser Ser Ala Val Leu	Pro Ala Val Ser Leu Glu Val Pro Leu Thr	
	155	160 165
Ala Ser Val Thr Ser	Pro Lys Ala Ser Pro Val Thr Ser Pro Ala	
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Ala Ala Phe Pro Thr	Ala Ser Pro Ala Asn Lys Asp Val Ser Ser	
	185	190 195
Phe Leu Glu Thr Thr	Ala Asp Val Glu Glu Ile Thr Gly Glu Gly	
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Leu Thr Ala Ser Gly	Ser Gly Asp Val Met Arg Arg Arg Ile Ala	
	215	220 225
Thr Pro Glu Glu Val	Arg Leu Pro Leu Gln His Gly Trp Arg Arg	
	230	235 240
Glu Val Arg Ile Lys	Asn Ser Ser His Arg Trp Gln Gly Glu Thr	
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Trp Tyr Tyr Gly Pro	Cys Gly Lys Arg Met Lys Gln Phe Pro Glu	
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Val Ile Lys Tyr Leu	Ser Arg Asn Val Val His Ser Val Arg Arg	
	275	280 285
Glu His Phe Ser Phe	Ser Pro Arg Met Pro Val Gly Asp Phe Phe	

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Ala Glu Glu Ile	Pro Ser Arg Ile Gln	Ala Ile Thr Gly Lys	Arg		
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Gly Arg Pro Arg	Asn Thr Glu Lys Ala	Lys Thr Lys Glu Val	Pro		
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Lys Val Lys Arg	Gly Arg Gly Arg Pro	Pro Lys Val Lys Ile	Thr		
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Glu Leu Leu Asn	Lys Thr Asp Asn Arg	Pro Leu Lys Lys Leu	Glu		
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Ala Gln Glu Thr	Leu Asn Glu Glu Asp	Lys Ala Lys Ile Ala	Lys		
	380		385		390
Ser Lys Lys Lys	Met Arg Gln Lys Val	Gln Arg Gly Glu Cys	Gln		
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Thr Thr Ile Gln	Gly Gln Ala Arg Asn	Lys Arg Lys Gln Glu	Thr		
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Lys Ser Leu Lys	Gln Lys Glu Ala Lys	Lys Lys Ser Lys Ala	Glu		
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Lys Glu Lys Gly	Lys Thr Lys Gln Glu	Lys Leu Lys Glu Lys	Val		
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Lys Arg Glu Lys	Lys Glu Lys Val Lys	Met Lys Glu Lys Glu	Glu		
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Val Thr Lys Ala	Lys Pro Ala Cys Lys	Ala Asp Lys Thr Leu	Ala		
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Thr Gln Arg Arg	Leu Glu Glu Arg Gln	Arg Gln Gln Met Ile	Leu		
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Glu Asp Met Lys	Lys Pro Thr Glu Asp	Met Cys Leu Thr Asp	His		
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Gln Pro Leu Pro	Asp Phe Ser Arg Val	Pro Gly Leu Thr Leu	Pro		
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Ser Gly Ala Phe	Ser Asp Cys Leu Thr	Ile Val Glu Phe Leu	His		
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Ser Phe Gly Lys	Val Leu Gly Leu Asp	Pro Ala Gln Gly Cys	Ala		
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 <213> Homo sapiens

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 <223> Incyte ID No.: 4717936CD1

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<213> Homo sapiens

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<212> DNA

<213> Homo sapiens

<220>

<221> misc-feature

<223> Incyte ID No.: 079702CB1

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<210> 58

<211> 1627

<212> DNA

<213> Homo sapiens

<220>

<221> misc-feature

<223> Incyte ID No.: 116208CB1

<400> 58

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<210> 59
<211> 1043
<212> DNA
<213> Homo sapiens

<220>
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<211> 2448

<212> DNA
<213> Homo sapiens

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<211> 2255
<212> DNA
<213> Homo sapiens

<220>
<221> misc-feature
<223> Incyte ID No.: 320087CB1


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<212> DNA
<213> Homo sapiens

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<220>
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<223> Incyte ID No.: 491271CB1

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<210> 63

<211> 1185

<212> DNA

<213> Homo sapiens

<220>

<221> misc-feature

<223> Incyte ID No.: 585172CB1

<400> 63

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 <211> 2596
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 997067CB1

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<210> 66
<211> 1574
<212> DNA
<213> Homo sapiens

<220>
<221> misc-feature
<223> Incyte ID No.: 1443262CB1

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<210> 67

<211> 2197

<212> DNA

<213> Homo sapiens

<220>

<221> misc-feature

<223> Incyte ID No.: 1521648CB1

<400> 67

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<223> Incyte ID No.: 1685494CB1

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<210> 69
<211> 2785
<212> DNA
<213> Homo sapiens

<220>
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<223> Incyte ID No.: 1730829CB1

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 <211> 1231
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 <213> Homo sapiens

<220>
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 <223> Incyte ID No.: 1864641CB1

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cggccccctg agtgagtccg gtctcccggc gaaagtgagc gaggtttgac cggagcgcgc 240
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aacgtgaaaa acaactaaga gcatcaagaa gcactataga ttagctaaa catccatga 360
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 <213> Homo sapiens

<220> -
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 <223> Incyte ID No.: 2444604CB1

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<210> 72
 <211> 2332
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 2445008CB1

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ccgtggtgct ggtattgtaa tagagatttt gatgatgaga agatccttat tcagcaccaa 240
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<210> 73

<211> 1936

<212> DNA

<213> Homo sapiens

<220>

<221> misc-feature

<223> Incyte ID No.: 2572462CB1

<400> 73

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1936

<210> 74
 <211> 1667
 <212> DNA
 <213> Homo sapiens

<220>
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 <223> Incyte ID No.: 2572892CB1

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1667

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 <211> 759
 <212> DNA
 <213> Homo sapiens

<220>
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 <223> Incyte ID No.: 2785674CB1

<400> 75

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tcccagttcc ccaaggcacg ccttcttccc aggcagctct aacagccctt tcatgaagg 660
aatgctagtc ttctgtccat cagtgccatt tcctgtagaa cttaaaggctg ttccaagaat 720
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<210> 76
 <211> 1421
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 2797479CB1

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<400> 76
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catccccgat ccgaaccttc tcaagtagct gttgatagtg ctggagctcc acgggtgacat 180
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aattattctt cagcagcagg tccgtccagg agaaagcact gtcttgcccc tcaggccgaa 360
tgtacagcag atagaagcgc cagatgtcag cagggatccc cgtgtcctgg gctttgattt 420
tcctggttca gcacgaattc atgaaggaac tcacactcta gagaaacctt atgaatgtaa 480
gcaatgtggg aaattgttat ctcatcgctc aagctttcga agacacatga tggcacacac 540
tggagatggc cctcataaat gcacagtatg tgggaaagcc tttgactctc ctagtgtatt 600
tcaaagacat gaaaggactc aactggaga gaaacctat gaatgcaagc aatgtgggaa 660
agccttccgt acttccagtt cccttcgaaa acatgaaaca acacacactg gagagcaacc 720
ctataaatgt aaatgtggaa aagcttttag tgatttattt tcctttcaaa gtcattgaaac 780
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cacattcaga tacttgaaag aaataaatcc tgtgaatgta aacgtggtaa agccttaaga 1320
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<210> 77
 <211> 2386
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 2960640CB1

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<400> 77
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aagattttct ctctcattat tgcctcatc atagtctctg attgtctctt aaagtaagtg 2280
gtttatagac attactattt ctgataataa tttaaaact actataaaca aatttataaa 2340
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<210> 78
<211> 1432
<212> DNA
<213> Homo sapiens

<220>
<221> misc-feature
<223> Incyte ID No.: 3454051CB1

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<400> 78
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tccctggcg ggcatgcaga gcacaatggg aggccatact gccacaagcc atgctatggg 180
gctctctttg gacccagggg ccctcccat atgaagacat tcaactggga gacctcgctg 240
tgccctggct gtggggagcc cgtctatttt gctgagaagg tgatgtcatt aggcagaaat 300
tggcaccgac cgtgtctgag gtgccagcgt tgccacaaga cctgactgc tgggagtcac 360
gctgagcatg atggagtccc ctactgccac gtccctgct acggctacct gtttggcccc 420
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aaatgagacg ctcaaaaaa aggtcaccc aactcaggcc tcccatcatg cccctcatgg 540
tccaatggaa gctacaaaaa tctccagtc catgggggtt ggggaagggt ggatcttggg 600
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cctttcccat ttctatctgg ttagggaaca gcccgttttg aagggtatcc tctctctggc 720
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tattgaattt cagcctctgt ggcttcttca ataaaatgtt ggctcccatg ccttcaactc 840
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gaaagccaca tgcccaaggt cacacagcaa gttaatggtg aagggtttat cagagccag 1260
ggcagactca gtggcttctt atccagggct cttctcacag ctggtcacca ctgccccaac 1320
ccaaggggca cctttattta cagaatctcc ccaaccgtga gacgggtgcc agcagaccac 1380
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<210> 79
 <211> 1816
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc-feature
 <223> Incyte ID No.: 3510640CB1

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<400> 79
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agtttctgag gcaggagcat tccaggggga agcgtgggct ggaccaggat gtgcggtgac 180
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cttctcttcc caactcccag ccaccccttg aggtctatgt gagcctgac aaggcctgcg 540
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attcactggg aaaaaa 1816

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<210> 80
 <211> 1556
 <212> DNA
 <213> Homo sapiens

<220>
<221> misc-feature
<223> Incyte ID No.: 3815083CB1

<400> 80

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gttttctaac atataaaaac ctacagaaga agaaaataat tttctggatc aaattagaag 180
tctgtattat attgatgtct ccagattcaa atatattaga aagcagccgt ggagacaacc 240
atcttcattt tgggagaaat aactaaagcc cgcctcaagc attagaacta cagacaaacc 300
ctgatgcgac ctctccagat tgtcccaagt cgattgattt cccagctata ttgtggcctg 360
aagcctccag cgtccacacg aaaccagatt tgcctgaaaa tggctcggcc aagttcaagt 420
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ggtgttagtg cagaaagtgg tgttccgacc ttcagaggag ctggagggtta ttggagaaaa 540
tggcaagccc aggacctggc gactccccctg gcctttgccc acaaccctgc cggggtgtgg 600
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cagaacatcg atgagctgca ccgcaaggct ggcaccaaga accttctgga gatccatggg 780
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<210> 81
<211> 1951
<212> DNA
<213> Homo sapiens

<220>
<221> misc-feature
<223> Incyte ID No.: 3988457CB1

<400> 81

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ctccgattat gggataggag aagtgccctg ggagcccctg gatgtcccct taccctccac 60
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tggcgtgtc ggtggcacgt ttgaccgctt gcacaacgcc cacaagggtg tgctcagtg 180
cgcgtgcac ctggcccagg agcagcttgt ggtgggagta gcagacaaag atctgttgaa 240
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atctgctttg ggtcaaagag cccgtttctc catctggcaa ctctgtccat ccaaggggtt 1920
ttcgggttct cgggccaagg cccgggggtg g 1951
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<210> 82

<211> 1313

<212> DNA

<213> Homo sapiens

<220>

<221> misc-feature

<223> Incyte ID No.: 131890CB1

<400> 82

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cacatcataa aacctcccag gacataaagg tgagcacaga ccctgttttg atcaagtcag 180
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ggctgaagga actttgtcat cagtggctgc ggccagaaat aaacaccaag gaacagatcc 480
tggagcttct ggtgctagag cagtttcttt ccatectgcc caaggagctc caggctctggc 540
tgcaggaata gcgccccgat agtggagagg aggcctgac ccttctagaa gacttggagc 600
ttgatttatc aggacaacag gtcccaggtc aagttcatgg acctgagatg ctgcgaaggg 660
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tactaaaaat atgaaaatta gccaggcatg gtggcacatt cctgtaatcc cagctactcg 1260
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<210> 83

<211> 1197

<212> DNA

<213> Homo sapiens

<220>

<221> misc-feature

<223> Incyte ID No.: 238642CB1

<400> 83

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tgggtgatcc acagatagct ccttctctcc cgcccttcc ttttgtttg gaggtcccag 180
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gatctgtgtt cacagacatc tgggggaaga aaaggagcag gaaactaccc cgcacagagt 240
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aagtgcagcg tgccaaagag ggaggaaaaa cgcccgtatg gagaatttga acgccagcaa 360
acagaaggga atttttagaca gaggctgctt cagtctctcg aagaatttaa agaggacata 420
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75/91

SUBSTITUTE SHEET (RULE 26)

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 <212> DNA
 <213> Homo sapiens

<220>
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 <223> Incyte ID No.: 1441770CB1

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<220>
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<213> Homo sapiens

<220>
<221> misc-feature

<223> Incyte ID No.: 2101803CB1

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<213> Homo sapiens

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<210> 96
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 <213> Homo sapiens

<220>
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 <223> Incyte ID No.: 2117346CB1

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 <212> DNA
 <213> Homo sapiens

<220>

<221> misc-feature

<223> Incyte ID No.: 2119917CB1

<400> 97

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<212> DNA

<213> Homo sapiens

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<223> Incyte ID No.: 2123456CB1

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<223> Incyte ID No.: 2148792CB1

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<212> DNA
<213> Homo sapiens

<220>
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<211> 2196
<212> DNA
<213> Homo sapiens

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<220>
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<223> Incyte ID No.: 3282941CB1

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<400> 102

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<210> 103

<211> 749

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> 735, 736, 741

<223> a or g or c or t, unknown, or other

<223> Incyte ID No.: 3286656CB1

<400> 103

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<211> 1311
<212> DNA
<213> Homo sapiens

<220>
<221> unsure
<222> 1294
<223> a or g or c or t, unknown, or other
<223> Incyte ID No.: 3490802CB1

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<211> 990
<212> DNA
<213> Homo sapiens

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 <211> 1048
 <212> DNA
 <213> Homo sapiens

<220>
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 <212> DNA
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<220>
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 <212> DNA
 <213> Homo sapiens

<220>
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KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,
MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
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Published:

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- Before the expiration of the time limit for amending the
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For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: NUCLEIC-ACID BINDING PROTEINS

(57) Abstract: The invention provides human nucleic-acid binding proteins (NuABP) and polynucleotides which identify and en-
code NuABP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also
provides methods for diagnosing, treating, or preventing disorders associated with expression of NuABP.

WO 00/44900 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/02237

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C12Q1/68 C07K14/47 C07K16/18 G01N33/68
A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K C12N C12Q G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HILLIER ET AL.: "The WashU-Merck EST project" EMBL DATABASE ACC NO: R73178, 29 June 1995 (1995-06-29), XP002139426 abstract	1-15, 17, 20, 23
X	WO 95 14772 A (MATSUBARA KENICHI ; OKUBO KOUSAKU (JP)) 1 June 1995 (1995-06-01) page 394 - page 395	1-15, 17, 20, 23
A	JANSEN ET AL.: "Preferential binding of yeast Rad4.Rad23 complex to damaged DNA" THE JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 50, 11 December 1998 (1998-12-11), pages 33111-33114, XP002139427 page 33111, column 2; figures 1-4	1-17, 20, 23

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"Z" document member of the same patent family

Date of the actual completion of the international search

6 June 2000

Date of mailing of the international search report

27.09.00

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van Klompenburg, W

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/02237

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 856 128 A (HAWKINS PHILLIP R ET AL) 5 January 1999 (1999-01-05) column 2, line 8 - line 34; claims 1-6 ---	1-17,20, 23
A	US 5 206 152 A (SUKHATME VIKAS P) 27 April 1993 (1993-04-27) column 1, line 11 - line 22; claims 1-12; example 8 ---	1-17,20, 23
A	GRISHIN N V: "The R3H motif: a domain that binds single-stranded nucleic acids" TIBS TRENDS IN BIOCHEMICAL SCIENCES,EN,ELSEVIER PUBLICATION, CAMBRIDGE, vol. 23, no. 9, 1 September 1998 (1998-09-01), pages 329-330, XP004146825 ISSN: 0968-0004 page 329, column 1; figures 1,2 ---	1-17,20, 23
A	MOROZOV V ET AL: "A putative nucleic acid-binding domain in Bloom's and Werner's syndrome helicases" TIBS TRENDS IN BIOCHEMICAL SCIENCES,EN,ELSEVIER PUBLICATION, CAMBRIDGE, vol. 22, no. 11, 1 November 1997 (1997-11-01), pages 417-418, XP004094961 ISSN: 0968-0004 page 417, column 1; figures 1,2 ---	1-17,20, 23
P,X	WO 99 33982 A (CHIRON CORP ;HYSEQ INC (US)) 8 July 1999 (1999-07-08) page 2, line 28 -page 3, line 15; claims 1-22 -----	1-14

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/02237

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claim 16 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 18, 19, 21, 22
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Claims 1-23 (all partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 00/02237

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 18,19,21,22

Claims 18,19,21 and 22 refer to an antagonist and agonist of the polypeptides without giving a true technical characterization. Moreover, no such compounds are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 5 and 6 PCT). No search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/ US 00/02237

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Invention 1. Claims: 1-23 all partially

An isolated polypeptide comprising an amino acid sequence of SEQ ID NO:1 or a naturally occurring amino acid sequence having 90% sequence identity thereto or a biologically or immunogenic fragment of SEQ ID NO:1. An isolated polynucleotide encoding said polypeptide, preferably of SEQ ID NO:56 or with at least 90% sequence identity thereto or a complementary polynucleotide. A recombinant polynucleotide comprising the above mentioned polynucleotide linked to a promoter sequence. A cell transformed with the recombinant polynucleotide and a transgenic organism comprising said recombinant polynucleotide. A method for producing the above mentioned polypeptide. An isolated antibody binding to said polypeptide. A method of detecting a target polynucleotide. A pharmaceutical composition comprising an effective amount of the above mentioned polynucleotide. A method of treating a disease, comprising administering the above mentioned pharmaceutical composition. Methods of screening for compounds that can act as agonist or antagonists or that alter the expression of said polypeptide, pharmaceutical compositions comprising these compounds and methods of treatment using these compositions.

Inventions 2-55: Claims 1-23 all partially

As invention 1 but for the polynucleotide sequences of SEQ ID NOs:57-110 and the corresponding polypeptide sequences of SEQ ID NOs: 3-5,7-14,16-31,33-34,36-40,42,48,50-55 as far as applicable.

For the sake of conciseness the first subject matter is explicitly defined and inventions 2-55 are defined by analogy thereto.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/02237

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9514772 A	01-06-1995	AU 8116494 A	13-06-1995
		CA 2153480 A	01-06-1995
		EP 0679716 A	02-11-1995
US 5856128 A	05-01-1999	US 6015788 A	18-01-2000
US 5206152 A	27-04-1993	US 5763209 A	09-06-1998
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